



National Training Day: Report January 2024



*Together, we're finding
answers to cancer.*

Supported by



Prof Jarushka Naidoo

Beaumont RCSI Cancer Centre



Dr Grainne O'Kane

TCD St James's Cancer Institute



Angela Clayton-Lea

Cancer Trials Ireland



ACTIONS, NOT WORDS

When the opportunity for the National Training Day arose, we agreed that as well as providing a platform for expert opinion, shared learning, panel discussion and exploring needs and supports, that the event should result in clear outcomes and agreed actions.

Thanks to your engagement and openness on the day, we achieved that goal. Rather than list the actions in the conclusion, we believe they belong at the start (see: next page), because that is our focus: action over words.

We hope you enjoy this report and hold us to account on our stated intentions!

Jarushka, Grainne & Angela

The National Training Day 2024 was supported by an unrestricted grant from:



What happens next:

ACTION: Inform CTI focus for 2024 - **Achieved**

- An immediate outcome from the day was feedback to CTI's Strategy Day in late January, arising from which four key priority areas were agreed with the Board: **GDPR, Funding, Operational Efficiency and Clinician Engagement.**

ACTION: Progress report at every DSSG meeting - **Achieved**

- This began on March 22nd when the Board of CTI shared slides pertaining to the priorities, including milestones, and future actions.

ACTION: GDPR

- There is an urgent need for harmonisation of DPIA templates and interpretation of current GDPR legislation. A small sub-group will undertake a series of high-level actions in support of the community's need to streamline processes impacted by GDPR issues. Patients' views will be sought and presented to the Data Protection Commission as part of this exercise.

ACTION: Funding

- The need to secure increased funding support is paramount. Maximising existing funding opportunities and securing new funding streams requires increased efficiency, collaboration, and greater engagement with EU funded projects. Learning from other groups e.g., ETOP, and lobbying for government support is essential. CTI will provide a voice for learnings from the current HRB grant model – this will be explored further as part of the CTI's Retreat on May 10th.

ACTION: Lean processes

- The metric that matters most is 'Time to First Patient'. The timeline for opening a new study is key in making Ireland attractive globally - concerted efforts will be made to reduce this timeline including optimising operational efficiency within CTI and working collaboratively to minimise external delays.

ACTION: Clinician engagement / Mentorship

- Mentorship for all stages of a clinician's career is needed, including general clinical support and specific mentorship on research. This was discussed during the Stakeholder Meeting at the March 2024 DSSG to obtain further feedback. CTI will develop an induction pack, provide regular updates at DSSGs on funding opportunities and 'open calls' (and throughout the year via a 'live' funding section on the cancertrials.ie website).

ACTION: Site team engagement / Fortnightly site meeting - **Achieved**

- The theme of collaboration & shared learning arose again and again in the Operational Training session. CTI has begun to host a fortnightly virtual meeting that is open to all site staff. The meetings will be an opportunity for Research Nurses, Data Managers and Trial Coordinators to ask questions of their peers and CTI staff, share experience, identify best practice, and explore opportunities for further collaboration across research units.

ACTION: Inter-site communication / Newsletter

- Arising from the success of existing newsletters from SVUH, UHL and others, CTI will produce a bimonthly newsletter to showcase site activity, with the aim of increasing awareness and boosting interaction.

Angela Clayton-Lea

Acting CEO, Cancer Trials Ireland



CTI's 5-year ambition for cancer clinical trials in Ireland

The acting CEO of CTI, Angela Clayton-Lea, opened proceedings by outlining CTI's five-year ambition for cancer clinical trials in Ireland. She emphasised the need to focus on CTI's "core business" - bringing more studies to Irish trial sites and providing more access to novel drugs and treatments for clinicians and patients.

"CTI is at the centre of the national picture when it comes to clinical research," said Ms Clayton-Lea, explaining that it has over 200 stakeholder members, that span patient advocates, industry, funders and media, as well as clinicians and healthcare professionals.

Key strategic objectives underpin its operation, such as maximising its contribution to the national cancer strategy. Building a breadth of optimal, stable and scalable talent to serve growth is also a priority, she said; "we want to provide you with the best team we can from within CTI." Clinical research must be positioned as a fundamental part of clinical care through thought leadership, advocacy, and influence, noted Ms Clayton-Lea; "it cannot be just an add-on."

CTI must also remain financially stable and funded for growth. In terms of funding, 22 per cent is currently provided by the Irish Cancer Society, while collaborative groups such as

international consortia and pharma provide 41 per cent and the Health Research Board (HRB) provides 20 per cent. Philanthropy currently accounts for 14 per cent of funding and Ms Clayton-Lea affirmed that the goal is to further develop the core funding base so the organisation is less reliant on philanthropy.

CTI enrolled over 1,400 patients in clinical trials in 2023. Adopted industry studies account for the majority of CTI's study portfolio and academic collaborations are about a third. Investigator-led trials account for only 10 per cent but the hope is to grow this proportion, she noted. Interventional studies are a major focus, as these offer patients access to the very latest drugs and innovations.

The well-documented National Cancer Strategy goal is to have six per cent of patients enrolled on clinical trials annually by 2026. Yet there are many hurdles to achieving this, said Ms Clayton-Lea. "We cannot address this ambition without addressing the challenges."

The process and timeline for opening a trial is a multistep process that is lengthy and onerous - some 25 steps are involved between the initial concept and its official opening.

The complexity has grown in recent years, added Ms Clayton-Lea. The goal is to ultimately streamline this process. CTI's cancer trials management system (CTMS) is about to go live and this will help with developing trial targets and timelines, as well as enabling comparison of timelines across like for like studies. She noted while regulatory submissions can involve extended timelines, the new system Clinical Trials Information System (CTIS) incorporates defined timelines so this will have a positive impact. Consent from patients for future research can also be time-consuming, as can patient information leaflet (PIL) amendments. On the latter there is significant work being done on a template that will meet these requirements. Contracts also take a considerable amount of time and again, standardisation of templates is needed. Irish trials organisers must be able to set clear targets for timelines because "right now it's as long as a piece of string", she admitted.

In relation to study type and site selection, more cancer data analysis is needed and Ms Clayton-Lea referenced the positive work being done through the eHealth Hub. "This means we can look at the types of studies we should be attracting into Ireland based on reliable data around patient cohorts and the geographical presentation of patients." The site selection system has to be transparent, she added. A reliable mechanism is also needed for recording referral patterns, as cross-referral can make or break studies. "The aim is to support data driven trial selection, streamline processes, accurately record referrals, and encourage emerging investigators to engage with research."

“Some 25 steps are involved between the initial concept and its official opening... The goal is to ultimately streamline this process.” Angela Clayton-Lea

The collation of accrual metrics requires development and CTI is aiming to encourage collaboration towards a single metrics reporting system, and lobby for funding to support implementation of an electronic trial master file (eTMF) - some sites have been able to do this but it requires funding, noted Ms Clayton-Lea. Collaboration will enable this - the CRF-UCC developed portal has been successful and now Galway have shown interest in using this. “If we can provide the right tools then people will share and collaborate.”

Ultimately the aim is to bring more studies to Irish sites. To achieve this, Ireland must be as efficient as possible, optimise collaborative opportunities and support phase I studies as well as becoming the “go-to” country in Europe for conducting cancer clinical trials by leveraging our reputation. Access to genomic and genetic testing will be key - the ALIGN consortium PEACEPLUS will hopefully enable this. CNS, surgical and rare diseases have been identified as key areas for expansion.

Funding, however, is the major challenge. The HRB funding system sees hubs and sites in competition for accruals and there are ongoing efforts to encourage referrals between sites. “We need to move forward with one voice.” The

funding mechanism also means that CTRU resources are challenging and there is a lack of security for clinical trials staff. There is a Catch-22 situation, whereby clinicians lack protected time to carry out research but investigator-led trials find it difficult to secure funding. Pharma funding must be optimised and Ms Clayton-Lea suggested researchers are not capitalising on valuable partnerships. This is further undermined by a fundamental lack of political support for research, she added. “CTI’s goal is to work collaboratively with influencers to address funding deficits and leverage the pharma base,” she said, suggesting that industry could contribute a percentage of their profits towards research in Ireland. “CTI wants to operate within a landscape that meaningfully supports strategic development and ultimately provides greater autonomy.”

Following her presentation, a discussion took place regarding the collection of data and the lack of a single system that would allow for routine and accurate capturing of relevant data across all sites. Specific funding and sufficient collaboration across the hubs will be needed to come up with one system, said Ms Clayton-Lea who added that the CTMS will provide “live” data.

More than 120 members of the clinical research oncology community attended the National Training Day, with another 100+ people attending online.



Dr. Karen Crowley

Health Research Board



An opportunity for funding cancer clinical trials

The HRB has a strategic objective to fund research that makes a difference and is focused on building and creating a thriving research environment in Ireland, said Dr Karen Crowley.

The aim of the Definitive Intervention and Feasibility Awards (DIFA) is to provide benefits to patients, people's health, and health service through support of studies evaluating a full scale definitive trial of an intervention or standalone feasibility studies conducted in preparation for a future definitive intervention, explained Dr Crowley. The cancer stream of the DIFA grants was introduced in 2023, with €3m set aside, and this is aligned to the HRB investment in cancer clinical trials infrastructure. Dr Crowley pointed out that these are not prescriptive, with no restrictions on design but rather a focus on quality. An intervention study can look at the efficacy, effectiveness, cost and broad impact of an intervention which could be a medication or medical device, occupational therapy, physiotherapy, radiation therapy and others, as well as behavioural and psychological-based therapies. Evidence from feasibility studies is required to progress to full scale intervention study, she said; feasibility studies address any uncertainty around the main trial and

focus on feasibility outcomes rather than the clinical effectiveness of an intervention. For this, clear plans for progression to a definitive intervention (DI) study are required, however. The DIFA grants also fund trial methodology research as per its studies within a trial (SWATs) initiative but these cannot be funded separately.

There have been four rounds of DIFA since its introduction in 2017, with about €32m across 45 awards made to date, including 22 feasibility studies and 23 DI; Dr Crowley noted that two previously funded feasibility studies were funded as DI in the latest round. "This was really positive for us as we could see the studies working through the pipeline we have established with the DIFA awards." DIFA has a monitoring and evaluation framework to ensure and improve quality of HRB funded trials and the results of these are publicly available on its website. The next round of DIFA is expected to launch in late 2024 or early 2025, pending board approval, and it is expected that there will again be a cancer stream. Dr Crowley told the audience that the HRB would strongly encourage proposals in this area and she encouraged PIs to engage with clinical trial infrastructures early in their proposal development and focus on networking and communication with all the cancer groups throughout the year. She added in the post-presentation discussion that the model is working well and there had already been learnings between the cancer groups and the clinical research facilities, with information sharing ensuring groups are learning from each other.

Dr Crowley added that DIFA/HRB invest a lot of time in gathering a broad spectrum of reviewers, and this means that there is a period of time - over a year in the last call - between the call opening and contracts being signed. "This is a very detailed process and the aim is to ensure a broad spectrum of reviewers." Dr O'Kane said this timeline is "challenging" in oncology given how fast the field is moving. This was echoed by Prof Roisin Connolly, who said "depending on our area of research sometimes the timelines are not quick enough". She added that some trials can be funded through one mechanism, but with many of the trials clinicians want to do that will ultimately improve survival or improve treatment options, a challenge is that they are often multimillion in terms of funding, especially in the case of multi-site and collaborative trials. This requires "a lot of energy and time", yet there is a lack of protected research time for clinicians, and in some cases despite the time and effort involved, "it may not even come to fruition".

Sarah McGrath

Patient Consultants Committee



Prof Ray McDermott

Clinical Lead, Cancer Trials Ireland



Clinical trial involvement from a patient perspective

Patient advocate Sarah McGrath and Professor Ray McDermott (vice clinical lead of CTI/SVUH and TUH) discussed the realities of clinical trial involvement for patients. Ms McGrath is a breast cancer survivor and current participant in University Hospital Limerick in the Add-Aspirin non-recurrence trial.

Prof McDermott noted that the landscape has changed in recent years when it comes to patients and clinical trials in Ireland, saying he sees patients advocating for themselves when it comes to accessing trials. "Now the patient is very much part of all the decision-making and even the design of the studies which is hugely important and a major positive step." The challenge, however, is for the patients to understand some of the concepts that we are trying to develop in the scientific realm. This can be tricky, he admitted, and he said oncologists could be better at explaining these.

In relation to the challenges of trial recruitment, Ms McGrath said patients may find it difficult to think of clinical trials when digesting the news of their cancer diagnosis. Information on clinical trials should be disseminated to partners and family members as their views and opinions may impact on the patient's decision. A broader public awareness campaign is also needed, she added so there is more general knowledge in the population about trials.

While naturally patients and clinicians will have different perspectives, the initial approach to take part in a trial can set the tone for the entire process, so this must be considered. Prof McDermott highlighted the "huge role" the nurses play in educating and communicating with the patient. Both commented on PILs becoming longer and more complex - this is unhelpful for most patients. "We need plain English while still understanding that they are complex," said Ms McGrath, noting that there are approaches in other sectors to plain English versions or summaries of complicated topics. She added that conversations about clinical trials should be normalised so that patients don't assume these are only being suggested as a "last chance". Patients should not feel like they are being experimented on - some trials can be quite straightforward, she added. Yet there should also be awareness of the significance of taking part in a trial even when treatment is finished, as she is - this can be psychologically demanding

Ashley Bazin, team leader on the Oncology & Haematology Clinical Trials at Tallaght University Hospital (TUH), said it is highly individualised and different patients have different attitudes to clinical trial participation - some will have lots of questions, otherwise will sign up regardless. In her experience, only a small percentage of patients will decline to take part in a trial but she agreed that language is important. "We are focusing more on informed consent as it becomes more complex... Patients need to understand that this isn't their last option, this is a good medical option for them specifically."

How to ensure patient advocates are truly representative was also discussed and it was noted that some patients will find public advocacy activities easier than others but there are different types of contribution that can be made. Ultimately it is about engaging with all patients and making trials as accessible as possible.

Prof John Kennedy

Trinity St James's Cancer Institute



Clinical trial targets based on the National Cancer Strategy and OECI accreditation

Professor John Kennedy (Co-Director of the Trinity/St James's Cancer Institute) spoke of the "ferocious difficulty" involved in reaching the targets set by the National Cancer Strategy 2016-2026, namely that six per cent of patients with cancer onto therapeutic trials annually. The Organisation of European Cancer Institutes has a target of 10 per cent of patients recruited to prospective interventional clinical trials in the index year for each individual centre; he noted that this does not refer to patients on cohort observational biomarker driven studies, which has been a "fruitful area of recruitment" in recent years.

A target is important as it focuses attention: "Once you recognise you have a problem it starts to solve itself because you focus on it." These targets should be treated separately, he said, but the common denominator is new patients. Exactly who these are must also be defined; for example, other countries do not count non melanoma skin cancer patients - these should not be included in his opinion, as the majority will be cured by surgery.

In terms of what is preventing Ireland and its institutions reaching these targets, there are myriad hurdles, some of which are unavoidable and others that could be addressed and improved. Ireland's relatively small population does not lend itself to large scale studies and this cannot be changed

but there are many improvements that could be made to our cancer clinical trials infrastructure. "The absence of recognition, funding and clear paths of progression for people and research staff represent significant impediment to research and a lack of recognition of research within the health service," said Prof Kennedy. "It needs to be seen as a relevant, vital and critical activity."

Clinical trial offices tend to function at the edge of the health service - funding is insecure, contracts are temporary, and staffing is minimal. "When an individual is unavailable because they are ill, the whole thing falls apart - that should not be the case, it should be a core hospital activity." Very little progress has been made in addressing these issues; the current funding mechanism for staff in clinical trials units is via recurrent iterations of HRB grants - this has resulted in a proliferation of temporary positions that are unattractive to highly trained staff. "The NCCP and National Cancer Research Group should examine these mechanisms to ensure that newly appointed consultant cancer specialists have truly protected time to pursue research interests in their new posts," he said, noting that consultants appointed to a role within an institution heavily involved in research is a fundamentally different post to one in an institution where this work does not necessarily take place.

Irish clinical research is also taking place in a regulatory environment that is oppressive, and Prof Kennedy said his belief is that the "true purpose of GDPR has been lost", with a lack of clear governance leading to further problems. In terms of who can advocate on this, patients are powerful and can be very influential, he said.

In terms of local efforts to increase trial participation, Prof Kennedy said he strongly believes that clinicians must aggressively integrate trials into MDT meetings; "the question should be asked, 'is there a clinical trial this patient would benefit from?'" he said.

Ireland must also look to untapped areas for recruitment, such as surgery, while survivorship is a growing area. HSCP colleagues will be "invaluable" in achieving this, he said, concluding that "none of this will happen without people". "Ireland has a tremendous advantage in that our people are phenomenally well-trained, enthusiastic, collaborative, and at the forefront of what they do."

In the ensuing discussion, it was noted that the increased complexity and demands of trials has hindered recruitment, as has the especially restrictive eligibility criteria of pharmaceutical-sponsored trials. Regulation and compliance challenges make this even more difficult, agreed Prof Kennedy. Dr O'Kane emphasised the need to bring trial units together to achieve these targets. Prof Connolly reiterated the need to see research as a clinical service and not a bolt on to anything else. She also highlighted the importance of developing a portfolio of investigator-led trials where they can provide the eligibility criteria and know the population and thus design trials that can accrue a greater number of patients.

Claire O'Donohoe

Children's Health Ireland



Enabling efficient development/activation of clinical trials in Ireland

Claire O'Donohoe is the Clinical Trial Start Up Manager jointly appointed between Children's Health Ireland (CHI) and In4Kids, the Irish Network for Children's Clinical Trials. She discussed the myriad elements involved in the Clinical Trial of an Investigational Medicinal Product (CTIMP) start-up process.

Many people believe a protocol, ethics approval and regulatory approval are all that is required to open a clinical trial recruitment at site. However, she highlighted the number of key steps that not all are aware of, that must be completed in the background. Following receipt of a protocol, reviewing feasibility and resources should be the first step, followed by ethics approval and, regulatory approval. In parallel, there is also the need to focus on data protection, pharmacy, imaging, local lab, insurance and indemnity, vendors, budgets and contracts before opening recruitment. "There is a lot of detail in every element - it gets messy," she admitted, likening the process to a game of snakes and ladders.

Unfortunately, none of these steps can be skipped but there are efforts being made to streamline the process and invoke set timelines. "This is not skipping steps, but ensuring everything is working together in parallel." Solid feasibilities are essential, she said, given that this will impact the trial for

its entire duration. DPIAs are difficult but also essential, and can be a major bottleneck and problem. Again, efforts are being made to improve the DPIA process, and a national template is coming, hopefully sooner rather than later. "We need to keep pushing for it." In the meantime, a good relationship with the relevant Data Protection Officer is key; "it doesn't make it any faster but just means I know what I am doing at every stage," said Ms O'Donohoe.

The research ethics process improved with the establishment of the NREC in 2020, which provides a single approval even if multiple sites are involved in a clinical trial. In January 2022, the new EU clinical trials regulation repealed the old clinical trials directive and the CTIS was launched. This means clinical trial authorisation can be applied for in up to 30 European countries with a single application. The CTR establishes a timeline of 60 days for member states to evaluate a single application, Ms O'Donohoe explained. "This timeline can be extended if requests for information happen - that generally does, but the max is 106 days," she said, adding that the CTIS is of "real benefit". The ACT-EU (accelerating clinical trials in the EU) initiative is also bearing fruit; for example, from January 1, 2024, NREC no longer charges fees for applications submitted by non-commercial sponsors of trials. A total 76 clinical trials across disease areas were authorised under CTR since 31 Jan 2022, in contrast 532 clinical trials were authorised in Neoplasms in Europe in the same time period "This shows how many are out there that we are not in," Ms O'Donohoe pointed out.

Improvements are being made to clinical trial agreements, such as the IPHA template introduced in 2021 and the HSE model clinical trial agreement in 2022, which will hopefully be updated in 2024. Trials must also be budgeted accurately, she said. "Everything always requires more resources than is estimated - budgeting must be realistic."

Enabling efficient development of clinical trials in Ireland will require communication, consistency and culture, said Ms O'Donohoe. "We need ample internal, external and patient communication and we need to engage early and often." She also criticised the increasing complexity of PILs and said there needs to be more flexibility with respect to this. Crucially, the culture must be there, she said. "Culture eats strategy for breakfast. We need our KPIs, data and deliverables but without the team to execute that there is no point. Everybody needs to have the same view."

During the discussion that followed, it was pointed out that there is no financial comeback when a pharma company pulls a site because recruitment has been achieved elsewhere and they decide not to open in Ireland. Ms O'Donohoe noted that start up contracts are being explored. "These are not simple and not every company will work with them but there is increasing recognition of the man hours that go into feasibility and ethics."

Prof Aisling Barry

IRROG



Prof Aoife Lowery

University of Galway



Roadblocks to opening trials / existing supports / additional assistance required

The various roadblocks to opening clinical trials were discussed and further elucidated by Professor Gerry Hanna (Queens University Hospital), Professor Aisling Barry (Irish Research Radiation Oncology Group (IRROG) and Professor Aoife Lowery (University of Galway).

According to Prof Lowery, in her own experience delays have been as a result of contract issues, as well as DPIA and GDPR but also staffing problems. She reiterated that people working in CTUs are often on short term or temporary contracts. "They come on board, get trained up and then get attracted out to industry where the conditions are better and salaries are higher - it's an ongoing problem." Prof Hanna agreed there is a

pressing need to build a dedicated workforce of clinical trials staff who are offered contracts on par with core staff.

Prof Barry echoed this, saying her unit has seen a huge turnover in staffing for similar reasons. Funding also represents a major roadblock in radiotherapy trials, as the lack of pharmaceutical industry funding means it is difficult to open and fund these types of studies. Early start-up funding is a particular stumbling block. The recent establishment of IRROG, however, has significantly changed how patients can access radiology studies within the country. "It means that all patients should have access to any radiotherapy trial available and has helped us overcome that roadblock."

Funding for surgical trials is a similar challenge, Prof Lowery said, as it also lacks the pharma funding stream. The UK has established a surgical trials network and there are many trials there that Ireland could be recruiting to, yet funding is the barrier. "We need a new mechanism to allow us to open surgical clinical trials to cancer patients in Ireland - a surgical trials network here in Ireland would be welcome," she said.

On a positive note, access to the necessary technology is improving, Prof Barry noted; while Dublin invariably had the most advanced technology for many years, now Cork and Galway have new units with similar technology. Yet more collaboration is needed, especially on multidisciplinary trials which can be more challenging. Prof Lowery said that, from a surgical trials perspective one of the biggest challenges is motivated PIs; "They don't have the time to dedicate to what needs to be done to get a trial over the line."

Dedicated time for researchers and investigators is a huge roadblock; Prof Barry noted that her post and a new post in Trinity College Dublin are the only two academic positions in the country with dedicated time. "We do research because we love doing it and we want to help patients but it needs to be recognised and supported." She also echoed Prof Kennedy, saying that this dedicated time needs to be there from the beginning of their contract so that an established clinical practice is not disrupted. "Clinicians need to grow their clinical and academic practice together."

Prof Lowery said that funding mechanisms in Ireland mean there is an element of competition and this is stymying collaboration between centres. This is especially true in the area of rare diseases, she added, where referral between centres is key due to the limited number of patients in this population.

Talking about clinical trials should be an everyday conversation for every patient, Prof Barry said. "No matter what discipline or clinic you are going into, there should be something available for you."

Thank you to Prof Ger Hanna, Queens University Hospital, for chairing this session.

Investigator Training: Developing effective clinical trialists in Ireland



Dr Sinead Noonan, CUH



Dr Lynda Corrigan, TUH

Chaired by Dr Richard Bambury, this training session addressed the role of clinician-scientist from a number of different perspectives.

Addressing the question of work/life balance, **Dr Sinead Noonan** highlighted the importance of doing fewer things and doing them well, and that the idea that people can “have it all” is a fallacy that sets one up for failure. Prioritising must also include prioritising what things must NOT be done, and only saying yes to those things that already fit with your existing priorities.

Dr Noonan also highlighted the systemic inequity that exists in Ireland, arising from implicit bias and expectations. She noted the problem was particularly prevalent in media, where despite 81% of specialists in Public Health Medicine being women, just 30% of media guests speaking about COVID-19 during the pandemic were women. Dr Noonan described how inequity is structural, systemic and implicit, removing the opportunity for the subjects of inequity to redress the balance. She said that changes must be made at systemic and societal level, and decisions makers must come from diverse groups.

The question of work/life balance arose as part of **Dr Lynda Corrigan's** presentation about the needs and challenges faced by young investigators. Dr Corrigan noted the impact of family life and children on her career, before turning to the primary focus of her presentation, where she highlighted opportunities in Ireland - room for expansion, a range of funding options, existing infrastructure & guidance and a burgeoning Public & Patient Involvement environment.

Her description of challenges and needs included time pressure and clinical commitments, the shortfall in infrastructure in terms of fully staffed trials teams, and lack of protected resources. She also highlighted the time it takes to open trials, and the challenge this presents in relation to attracting collaborators to Ireland. Dr Corrigan also referred to the challenge of simply understanding all of the processes involved, be they around

funding trials or having them reviewed / approved at DSSG and so forth.

Her advice to other emerging investigators is to leverage mentorship as much as possible, by using your contacts, requesting meetings, and availing of conference / congress opportunities. Knowledge of the logistics of trials was also important, and underpinning all of this was the theme of collaboration. Collaborate formally with mentors, with your national and international peers and multidisciplinary teams.

This theme of collaboration was expanded by **Prof Roisin**

Connolly in her presentation about ‘Engaging Co-operative Groups & Designing Early Phase Trials’.

Under the heading ‘What do we need to succeed?’ Prof Connolly repeated the mantra of collaboration, and also outlined several other important areas which are addressed



Prof Roisin Connolly, CUH

below. One of these areas highlighted the need for an enabled critical mass of academic-clinicians, and she cited a Nature paper that described four headings under which to list the many challenges facing investigators.

From a personal perspective, clinician-scientists have inadequate incentives, and more expectation of a work-life balance. From a professional viewpoint, they face overwhelming clinical demands, long training periods of training compare with peers, and more attractive career opportunities (e.g. leadership positions) away from research. Institutionally, there is a lack of support, funding, mentorship and collaboration. Lastly, nationally and internationally there is a shortage of oncologists, often no recognition of the role of clinician scientist, a lack of investment in research, and a lack of formal training for the career path.

The other areas that are key to success, Prof Connolly noted, were:

- Strong clinical and administrative leadership
- Strategic priority development & execution (focus)
- Central & local core infrastructure: resourced, efficient, accountable, passionate
- Core national funding for clinical trial conduct & correlative analyses

- Support in obtaining charity and EU funding for clinical trials
- Train, support, mentor the next generation of investigators
- Partnership is ESSENTIAL: between patients, clinicians, basic and clinical investigators, industry, academic groups

Prof Connolly also listed some of the benefits of engaging with co-operative / collaborative groups, such as: -

- Being part of a Scientific/Academic Community
- Access to high quality trials for Irish patients
- Opportunities to develop & conduct Investigator-Initiated Studies
- Research Output: Grants, Presentations, Publications
- Training & Mentorship, Career Development

Prof Connolly used the US National Cancer Institute as a model of a national clinical trials network structure. NCI's National Clinical Trials Network (NCTN) is a collection of organisations and clinicians that coordinates and supports cancer clinical trials at more than 2,200 sites across the United States, Canada, and internationally. NCTN provides the infrastructure for NCI-funded treatment and primary advanced imaging trials to improve the lives of people with cancer. The NCTN consists of four adult groups and one large group focused solely on childhood cancers. The structure also includes a Canadian Collaborating Clinical Trials Network.

Finally, on the question of developing early phase trials, Prof Connolly noted that extensive collaboration and research support is required, including: Basic scientists, Clinical Pharmacology, Pharmaceutical Industry; Study Sponsors, Research Support, Biostats; Clinical Trials/Phase I Team; Investigators, Co-Investigators across sites/networks; Surgery (Pre-surgery drug exposure studies); Pathology (Biopsy/ Tissue analysis); Interventional Radiology (Tissue procurement).

Dr Austin Duffy & Dr Geraldine O'Sullivan Coyne presented on the START Phase I unit at MMUH. START stands for the 'South Texas Accelerated Research Therapeutics'. It is a physician-owned group founded in 2007 by oncologists to create a standardised program to accelerate cancer research. It is the largest phase I research group in the world, enjoys a strong reputation and track record, and has had over 150 high-impact publications in the past 10 years.

Overall, START has enrolled 10,000+ patients since inception, with 1300+ studies (completed and active), around 700 of which are first in human trials to date. START has 345+ dedicated employees and a 6 week turn-around time to study start up and accrual.

Dr Duffy worked to open this national service in Ireland to address unmet clinical need through a dedicated unit that will open phase I studies at scale for expertise, safety & training. Dr Duffy and Dr O'Sullivan Coyne noted how START provides supports around study acquisition & activation, regulatory



Dr Austin Duffy, Mater



Dr Geraldine O'Sullivan Coyne, Mater

affairs, budgeting & contracting, quality assurance, and information technology. The unit has been working from a temporary space in MMUH and will move to its permanent, purpose-built facility in MMUH in Summer 2024.

Finally, **Dr Robert Henderson** presented on the lessons learned from conducting CAR-T therapy trials in SJH. The first patient was infused with CAR-T in Dec 2021, and since then over 60 patients have been treated.



Dr Rob Henderson, TSJCI

It was immediately apparent the high degree of co-operation required between

numerous stakeholders nationally (regulators, pharma, NCCP) and within the hospital (corporate, laboratory, pharmacy, haematologists, ICU, neurology, nursing and administration). This gives rise to unique considerations in the implementation of staff training & SOPs for these trials.

CAR-T is a patient-specific product and is not available "off the shelf". CAR-T is essentially a 'living drug' and cell handling requires cryobiology lab involvement and considerable logistics for transport, processing and storage. This results in unique training requirements for all involved departments and bespoke on-boarding procedures as different companies apply different standards. The collection of cells for CAR T manufacture must be performed under tissue establishment authorisation from the HPRA. EPA licences may be required for clinical trials products that are not licenced as CAR T cells as they are classified as 'Genetically Modified Organisms'.

Ward staff required specific training in a dedicated in patient unit, in anticipation of known adverse events. Dr Henderson concluded by highlighting the expanding indications for CAR-T in clinical trials, with ongoing developments in new drug targets, new cellular constructs, and new immune cell types.

From the Q&A session which followed the above presentations, it became clear that there is a need to establish a mentoring programme for emerging investigators. It was also confirmed that as part of CTI's drive to become more streamlined (and in an effort to further support its members), development of an induction pack would be welcomed by emerging investigators.

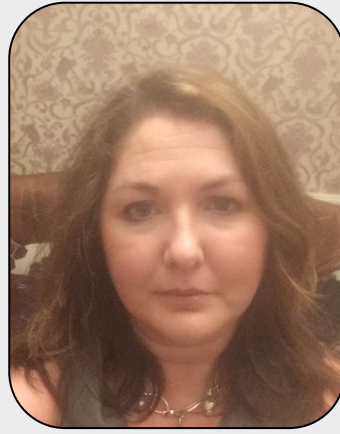
Operational training: Optimising operational excellence at Irish sites



Jo Ballot, SVUH



Ashley Bazin, TUH



Deirdre Lehwald, TSJCI



Maureen O'Grady, UHL

When given the opportunity, the participants in the Operational Breakout group demonstrated a willingness to share experiences and make suggestions and recommendations that underpinned the central theme emerging from this session: Collaboration between sites.

The sites recognised that sharing their successes is just as important as sharing the tools and methods they use to troubleshoot problems – because demonstrating the capacity to execute a trial well improves the likelihood of getting more trials in the future. Success breeds success.

In support of building such success stories, the participants described the practices, tools and platforms they used, and approaches varied from site to site.

The Mater reported having quarterly meetings with the CEO of the hospital to highlight the positive financial impact of trials on the hospital and suggested inviting the CEO to future national meetings and further drive home the value and importance of trials and research.

Meanwhile, some sites have access to platforms that include all relevant hospital departments on trials, and track blood test / scan / other items against deadlines. Others are forced to rely on paper-based systems, since the Ransomware attack. Within sites, the teams have developed bespoke tools like trial assessments form for each study (TUH) and a 'screening cheat sheet' that functions like a checklist with tips to aid new studies (Beaumont). Systems like these are then overseen by weekly emails, and monthly study meetings, all giving rise to a range of effective methods for conducting cancer trials.

Taking a higher level view, the group agreed that the practices

they use should be reflective, and collaborative. Trial processes could and should be mapped, shared and discussed, best practices identified and implemented, and then systematically reviewed in time.

In order to enable this, participants suggested an increase in inter-site communication. They also suggested supporting communications in the form of a national newsletter that could advertise what sites have to offer, be that patient referrals, or novel compounds, all aimed at boosting interaction.

Moreover, the participants recognised the need to communicate outside of the trial sites, with translational scientists for example, and with patient groups, and other experts in areas of patient population and more. Finally, the group talked about the challenges and delays associated with opening trials, and claiming back the resources used, even where a trial may not open.

Chaired by:
Maureen O'Grady
UHL

Discussion points from Operational Training:

Newsletters:

- Advertise what a site has to offer: referrals; novel compounds
- Aim to boost interaction
- Suggestion: A national newsletter to/for sites for improvement

Communication: Bridging the gap, e.g.

- Scientists for TM (ILCC as a model)
- What patient populations (have we? Are there?)
- More insight into current / future activity
- Make practice reflective, with collaboration among centres, troubleshooting, but also celebrating and sharing success stories, because doing a trial well = more trials in the future.

Patient support

- Working with external patient groups; patient-to-patient support groups

Process mapping exercise (on a site level initially)

- What works well / suggest changes / Implement changes / Review
- Shared learning between sites, egg collab between Mater & SVUH

Suggestion:

- Inter-site communication
- (by HRB cluster?) Facilitates relationship-building

Best practices:

- Support office for study start-up (Mater / Lisa)
- Invite CEO to national meetings
- Electronic reporting system for tracking patients
- Mater / quarterly meetings with CEO re: financial upside of running clinical trials
- "Training not required" form (BH)
- Would sites agree to accept study budget approved at other sites (saving on contract negotiations etc.)
- DPOs now not reviewing every DPIA – DP constraints
- Tracking patients on treatment / follow up

Best practice / troubleshooting

- TUH – assessment form for each trial – study specific requirements
- TUH – XL spreadsheet – categories for scans, bloods etc. highlighting timelines, updates per amendment (protocol v specific)
- TUH – Diary on ARIA, planning for bloods
- TUH – issues with kit inventory (complicated by expiring dates etc) – too many/few
- BH – screening cheat sheet, aim to prep for trial (checklist tips & tricks)
- BH – Weekly email to patient-involved departments – plan ahead, new patients consents
- SJH – Cancer Clinical Trials Planner (all relevant departments have access)
- UHL – Daily diary (paper, foolproof, i.e. cyberattack)
- HSE sites / delays with opening, may not be able to open a study – can we claim back funding for resources if study doesn't open / contract not signed? (ideally sign contracts early, to offset this).
- SJH – weekly trial meetings (discuss missing data etc.) – communication is key
- BH – Monthly team meetings – study issues, patients are not discussed
- High-level queries, pushback is sometimes required
- Data management / protected time for query resolution (may be time limit for query response, BUT may need PI input for response to resolve query)
- CRAs – please query during visits, don't look for lots of data post-visit (CRO CRAs)
- Benefit of having Trial Start Up Manager (per SJH)



Building a successful clinical trial portfolio for lung cancer

Chaired by:
Dr Sinead Noonan
CUH

Professor Jarushka Naidoo outlined the recent evolution of lung cancer clinical trials in Ireland that she has spearheaded since she became chair of the lung disease DSSG within CTI. A key element in building a lung cancer clinical trials portfolio has been understanding the population here, she said, explaining that she reached out to every lung cancer site in the country to understand the numbers involved and their demographics including age and geographical differences. Prof Naidoo co-led the largest comprehensive genomic analysis of non small cell lung cancer (NSCLC) in Ireland, which was published recently in the Journal of Thoracic Oncology. This involved over 2,050 patients, the biggest proportion of which have KRAS mutations, with a lower incidence of EGFR-related lung cancer.

She also sought to ascertain the level of interest in clinical trials and expertise in running trials. "Some PIs are particularly passionate in a certain area, and we have to go to where that passion is and foster that." There has also been significant work done to establish collaborations with cooperative groups such as ETOP, who have been welcoming and supportive, she noted.

The professor stressed the need to be "highly disciplined" about trial choices, including streamlining and being unafraid to say no to competing studies or niche trials where accrual will be low. She uses a scoring method to prioritise trials that she used in Johns Hopkins which evaluates them on various criteria such as academic credit or clinical impact. In terms of funding, she said 80% industry funding and 20% academic portfolio is the general rule of thumb in terms of developing a trials portfolio.

There are now a number of trials ongoing or opening soon in the early stage and advanced setting of NSCLC; Prof Naidoo explained that locally advanced lung cancer remains a niche but it is hoped trials will soon become available in this setting.

Trials opening in 2024 in the advanced setting include HARMONI3, MK-010, and ARCUS-10, all first-line, while LATIFY is now open to accrual in second-line all comers.

Prof Naidoo said it is clearly a priority to develop a KRAS programme in Ireland, as it is the most common genomic

subset of lung cancer and relevant trials include KRYSTAL-7 and ADEPPT, which will open in 2024.

The NEOCOAST2 trial was "a great example" of Ireland being able to participate in an academically driven but pharma-funded study that looked at utilising immunotherapy combinations in the neoadjuvant setting. "The evidence is building on offering upfront chemoimmunotherapy before surgery which is ushering in a new era for early stage lung cancer. There are currently no neoadjuvant chemoimmunotherapy options as standard of care - this trial allows us access to these novel agents but also allows us as an oncology community to become familiar with giving these treatments in the neoadjuvant setting."

Small cell lung cancer accounts for about 10% of all the thoracic malignancies and trials in this setting are also due to open, as are translational studies in areas including diagnostics and biomarkers of response to immunotherapy.

Maintaining a robust portfolio requires the creation of an ongoing dialogue between clinicians and scientists to foster collaboration; Prof Naidoo explained that the Irish Lung Cancer Alliance seeks to do just this and now has over 30 members. Forming strong partnerships and partnering with cooperative groups such as ETOP, EORTC, ECOG-ACRIN, and NRG has been essential.

Membership is one thing, but in-person engagement and networking is key, she said. "We cannot underestimate the importance of engaging with industry partners - the best way is direct PI engagement with global leads and MSLs."

Ireland must focus on delivering high quality results, by being careful about the trials that are selected and ensuring that they will suit our population and its demographics. In lung cancer that is going to be immunotherapy trials and KRAS trials, the professor said. Her goal for the future is to maintain an open clinical trial in each of the main therapeutic areas in thoracic oncology, and build a robust KRAS clinical trials and translational programmes.



Building a successful clinical trial portfolio for prostate cancer

Chaired by:
Dr Richard Banbury
CUH

CTI outgoing clinical lead Prof Ray McDermott outlined the ongoing efforts to build trial capacity and drive recruitment in prostate cancer clinical trials. Asking why we do clinical trials, he noted that well-known trial participants such as Booker prize-winning author Paul Lynch have spoken positively about their experience on trials and the difference it has made to their lives.

For clinicians, presenting the results of trials which will be practice changing, such as the ENZAMET trial, is a proud moment, noted the professor, but he said the resulting impact on patients with metastatic prostate cancer is much more meaningful. The benefits of clinical trials are myriad and far-reaching, as they include drug savings, individual patient care, enhanced quality of care, allowing clinicians to stay current, and to get used to using new medicines. Trials offer clinicians the opportunity to publish in major journals such as NEJM and The Lancet but also offer patients access to groundbreaking medicines such as PARP inhibitors

Echoing other speakers, he agreed it is important to network, both at home and abroad, in order to identify potential opportunities for Ireland. He pointed out that CTI can take on the role of sponsor for European trials and can open clinical trials in other countries - in this case, they helped to open ENZAMET in the UK, and also opened the companion study ENZARAD in five countries in Europe. "This non-traditional route is worth remembering."

Prof McDermott also noted that GDPR compliance has caused problems locally and attempts to streamline the associated processes would be welcomed. "We are only a small country and we will only attract trials to Ireland if we are nimble." Ireland is small, and thus relies heavily on cross-referrals, he added; this can work extremely well, such as with the NTRK/lorotrectinib study, which accrued seven patients, referred from all around the country - Ireland ended up being the biggest accruer in Europe for this trial.

Ten studies are opening this year in bladder, prostate and renal cancer. Genitourinary cancers roughly account for 10% of the entire accrual of clinical trials in Ireland, he said, and

this level of accrual has been consistent over the years. "In the last decade, more centres have become more interested and more expertise has come to certain centres so as we get more sites with GU interested clinicians, this accrual will go up," he noted, however, that not all trials are feasible to do in Ireland. The professor also cited the MK6482-011 study, which has already accrued 17 patients - a huge number - and involved lots of cross-referral. "This is a model of the collaboration that is possible."

We are only a small country and we will only attract trials to Ireland if we are nimble.



Building a successful clinical trial portfolio for gynaecological cancer

Chaired by:
Prof Con Murphy
Bons Cork

Just one per cent of trials in Ireland are in gynaecological cancer, noted Professor Donal Brennan but he stressed that new consultants in oncology have reinvigorated the gynaecology DSSG and this is set to grow.

Gynae oncology is quite a unique speciality due to the movement of patients between surgery and medical oncology and radiation oncology and back again, requiring significant integration of care, he explained. "We need to harmonise this so that trials can be offered to patients."

Collaborative groups are an important conduit to accessing surgical and medical interventions for patients, and have been instrumental in opening trials here in Ireland. Some hospital boards remain mistrustful of research, added Prof Brennan. "We need to push the idea that research improves clinical outcomes and we need research to become much more embedded in all our daily lives." This will improve patient outcomes, he said, but would also increase national and international institutional prestige and provide alternative funding streams.

The EU Cancer Mission brings added impetus to the area of cancer clinical trials, and this will result in a huge tranche of additional funding - some €4 billion. "We need to be ready to access that funding and be part of the collaborative networks that people are talking about." Integration of clinical research with basic and translational science must be increased, he added.

In terms of laying the groundwork for a robust portfolio in gynae oncology clinical trials, the professor noted that it took a lot of hard work in his unit in the Mater Hospital to get its ovarian surgery programme to the level required to open proper clinical trials. "We increased our primary site reduction rate and our complete site reduction rate quite significantly," he explained, adding that recently published data show how this has significantly improved survival in their ovarian cancer cohort. The groundwork gone into improving surgery means that they can now take part in major trials such as OVHIPEC-2, which is currently recruiting.

Prof Brennan also emphasised the importance of listening to patients, and advised finding out from patients what they

want. For example, patients consistently highlight the issue of menopause and the lack of data to support any intervention in menopause after cancer. That led to the Menopause After Cancer trial, which accrued 213 patients in just 16 weeks, showing the unmet need in this area. The outcomes from the trial interventions were significant and participants saw a major improvement in menopause symptoms - the trial won the Patient Advocate Award at ASCO in 2023. "These are the trials patients want to see - we need to focus more on survivorship and we need to provide evidence-based interventions for these patients."

We increased our primary site reduction rate and our complete site reduction rate quite significantly



Building a successful clinical trial portfolio for GI cancers

Chaired by:
Dr Michael McCarthy
UHG

With accrual in gastrointestinal cancers accounting for three per cent of the total, Dr Grainne O’Kane said there is still a lot of work to do in building this portfolio. She pointed out that a running theme throughout the training day had been collaboration, forming national frameworks and bringing scientists, medical oncologists, surgeons and other members of the cancer teams such as radiation oncologists together, and she spoke of her hope to recruit a surgical co-chair for the GI DSSG.

A challenge is that GI cancer represents a vast portfolio of multiple diseases - it almost encompasses too much, said Dr O’Kane. Yet a strength is the numbers of patients and the breadth of clinical trials that Ireland can get involved in. While there are targets that must be aimed for, the parallel goal is also to create change in terms of delivering clinical trials through empowering the patient.

Improvement is happening; access to clinical trials varies widely across Europe, she noted, and Ireland’s percentage growth in terms of numbers of clinical trials between 2010 and 2018 was the highest. “As more investigators return and build more momentum, we need to keep this momentum going.”

Again, collaboration will be key. Surgical/medical oncology and radiation oncology in GI must work together and Dr O’Kane said clinical trials units must come together and learn from each other; “CTI will have a huge role in building this framework.”

The focus must be on delivering trials at every step in the patient journey, from prevention through to survivorship. “Trials at every stage are essential but while we are aiming for survival and new treatments, we are also aiming for improved quality of quality of life.”

As in many other cancers, systemic treatments are being delivered earlier in GI cancers and there many more neoadjuvant trials coming through - this means the surgeon needs to be involved through the MDT structure, she said. “We do want to work together to deliver for our patients.” She agreed that cross-site referrals should be rewarded in later funding rounds so that more PIs are given opportunities.

Challenges in leading trials include changes in treatment paradigms, long accrual time, and lack of or delayed funding, explained Dr O’Kane. Yet the NEO-AEGIS study was one of the most successful investigator initiated studies in Ireland, and this trial saw accrual rates increased exponentially due to national and international collaboration. This is where our opportunities lie, she said. Translational studies are a “missing gap” within CTI but they are crucially important, she added.

“We need to know our population and what we can deliver at each of our sites so that we can focus on our strengths and ensure industry partnerships continue. Clinical trials in general bring up our standards and show improved outcomes for patients overall and the GI portfolio needs to deliver on its success of delivering in phase III and continue to attract industry partners.” Critical to this is understanding what prevents industry from opening trials here.

She concluded with key action points, such as identifying more GI PIs, naming local champions, building partnerships and increasing surgical engagement.

We need to know our population and what we can deliver at each of our sites so that we can focus on our strengths and ensure industry partnerships come back



An EU perspective / The ETOP experience

**Chaired by:
Prof Jack
Gleeson**

CRF-UCC

**& Prof John
Kennedy**

TSJCI

Professor Rolf Stahel president of the ETOP IBCSG Partners Foundation and former chair of the Comprehensive Cancer Center Zurich was at the meeting to outline how the European Thoracic Oncology Platform was initially developed and how it has evolved.

The original goal when it was first conceived in 2008 was achieving academic collaboration in Europe in cancer via an organisational structure. Warmly welcomed by most stakeholders, the professor said that the start-up funding came from individual hospitals, foundations, and clinical trial groups who were each asked to contribute €5,000.

A simple charter that promotes the exchange of ideas and research in the field of thoracic malignancies was drawn up and Prof Stahel notes the “immediate and extensive buy-in” from academic colleagues. Regular meetings were key in building the ETOP community - there are yearly meetings, yearly pathology and translational research meetings and yearly ETOP residential workshops. This also helps avoid them working in silos, noted Prof Stahel.

Now, the ETOP scientific committee meets once a month, and translational committee meets quarterly, the latter of which Ireland’s Professor Stephen Finn is the chair. The leadership committee meets every other week. The ETOP network now spans over 230 centres in 24 countries, having expanded to South Korea, Singapore, and Australia. Prof Stahel said there is a “very rich trial portfolio” and almost every trial is ETOP-sponsored

“Success begets success,” he said, and he cited the BELIEF trial which was one of those successes that helped build their reputation. “It accrued well, it published well and the primary endpoint was met, and it gave us a standard - deliver on time and show industry you can do it.”

The professor also noted the extended timelines in getting trials from concept to opening stage - for the AMAZE-lung study, the first discussion took place in September 2020, the protocol release was October 2022 and the first patient was recruited in March 2023.

“This is how long it takes. The important thing is to be resilient and not give up.” For those who wish to pitch a trial to ETOP, Prof Stahel urged clinicians to contact him or chair of the scientific committee Prof Solange Peters. Typically they will offer an invitation to present at the next scientific

meeting for feasibility considerations. ETOP together with the potential PI then develops a brief slide deck with design and statistical considerations and will contact a potential sponsor. If they are interested, a synopsis and draft budget are drawn up, and if agreement in principle is reached then protocol development and contracting negotiations begin.

Trials have to be patient-friendly - the professor said ETOP will not run a trial where the control group receives best supportive care. Even with the best of intentions, trials may not always work out, and Prof Stahel noted that ETOP has experienced a few trials that had to be closed prematurely. He also stated that learnings can still be gleaned from negative studies.

The structure of ETOP means there is the scope to do very innovative trials, such as the NICOLAS trial which looked at the addition of nivolumab to concomitant CRT in early stage NSCLC, which was the first to demonstrate that this is safe.

The professor also showed figures to illustrate that trials are expensive - even without patients. There are still huge costs involved in buying drugs, hiring personnel, monitoring and biomaterial collection, etc., even if no patients are accrued in the first year. Waiting even longer will be detrimental to the budget of the clinical trials group, he warned. “We do not receive government funding, we have to deliver, we have to have resolve and stay alive. Timing is essential.”

The professor concluded his talk by offering Irish clinicians some advice - he warned against focusing on the hurdles to carrying out research and urged instead a focus on reality and opportunities. “Concentrate on what can be achieved.” He elaborated on the lean governance structure in the context of trials. “We don’t have artificial levels - we have a scientific committee and the board, that’s it.” The executive committee has a small membership, meaning there is a small number of decision-makers. “Clinical trial activity is not a democracy - it cannot be, because you have to deliver and you don’t deliver if you sit in committees.”

Prof John Kennedy noted the broad CTI remit, which is national, multi institutional and multi disease. “That is a real challenge governance-wise and funding-wise and trying to be successful in all areas... This can mean we lack intrinsic focus.” Prof Stahel agreed, saying that as a group in a small country resources are limited and it is important to define priorities. “You can do anything but not everything.”



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