DSSG Digest

Winter 2019

The DSSG Digest has the most up to date news and listing of cancer trials and studies underway in Ireland.

cancer trials ireland

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Prof Bryan Hennessy, outgoing Clinical Lead, makes his summation after a 4-year tenure

As the outgoing Clinical Lead for Cancer Trials Ireland, I want to thank everyone inside and outside of the organisation for their support over the past four years. Those four years have seen a lot of change – some welcome, some less so.

As you are aware, we have come through a period of review with respect to organisation finances. I am pleased to report that we have made significant progress in this area. We have now established appropriate governance and controls around costings and reporting on our trials. In light of this progress, we are once again in a position to recommence evaluating new trials.

I am also delighted to have overseen the reshaping of the Clinical Executive Committee during my tenure. We have updated committee membership, the committee now meets more frequently (six times annually) by teleconference, all with the objective of enabling Principal Investigators to take a more active role in the running and decision-making of the organisation. I believe this approach is paying dividends.

During my tenure I have also tried to establish some early phase one trials, as I believe there is more that we can do in this regard, nationally. Cancer Trials Ireland has even developed some solid tumour phase one trials, which is not a traditional area for us, but one in which I hope we can grow into.

With respect to pancreatic cancer, I look forward to the outputs of the Gastrointestinal (GI) DSSG as to how we might use the funds recently raised. As I will become the Vice-Clinical Lead for the organisation for 12 months in 2020, I will assume the chair of the Scientific Management Group, where we will build on the work of the GI DSSG. In the short term, we have a new pancreatic trial using Paricalcatol that we hope to open in early 2020.

Finally, I wish to thank our CEO Eibhlín Mulroe for her support in my time as Clinical Lead. With Eibhlín's experience we were able to significantly, and effectively, step up our strategic advocacy with policy and decision-makers, and the healthy future of the organisation owes much to this work. I look forward to working with her to identify a new Vice-Clinical Lead for 2021 and beyond.

Prof Ray McDermott, incoming Clinical Lead, outlines his vision

I want to begin by acknowledging the organisation's gratitude to Professor Bryan Hennessy, who has helped to shepherd the organisation through a difficult period. Cancer Trials Ireland was subject to funding cuts, and as such studies were reduced. I am hoping to reverse that – and offer more studies across different disease areas in the coming years.

I believe we can achieve this through an increasing range, and scale, of funding streams that include the State, philanthropy, and fundraising. This should allow us to explore more investigator-led studies, reducing our reliance on industry-led studies.

In terms of the direction of cancer treatment and research, I think we can expect the environment to evolve in the established direction. Once-large disease areas will continue to be broken down into much smaller sub-disease types, but this does provide opportunities. One clear benefit is that we are now screening more patients in search of the rare, treatable mutations. As a consequence, we can treat certain patients with certain tumour types with the same therapy, irrespective of where the tumour originated.

Lastly, in terms of the cancer strategy, I note that Ireland is supposed to have increased clinical research – whereas in fact it has shrunk in recent years, due to funding cuts. It is vital that this government, subsequent governments, and ministers for health, recognise that clinical trials are budget-neutral and may even save the State money. Recognising this fact highlights the futility of reducing funding. In support of this, it is my desire to see the introduction of protected time for clinicians, security of tenure for research staff, and for acute care to recognise the value of research staff – and I will actively advocate on all of these points.

I look forward to working on your behalf as the Clinical Lead for the coming four years.

Pat Smullen and Horse Racing Ireland HAVE changed the face of Pancreatic Cancer trials in Ireland

In September, thousands of people donated money to Cancer Trials Ireland, supported by hundreds of people working at the Longines Irish Champions Weekend, but the truth is we can attribute the success of this incredible weekend to the popularity of one retired jockey – Pat Smullen.

Pat was diagnosed with pancreatic cancer in March 2018. Soon after his diagnosis he and his wife decided they would do what they could to support clinical trials for pancreatic cancer, and that triggered a humbling degree of support the likes of which Cancer Trials Ireland has never before experienced.

The scale and range of donations - from coins collected in buckets, to text message donations, right up to a one-off donation of €500,000 from Sheikh Hamdan bin Rashid al Maktoum. We had everything in between too, including the support of sports stars Shane Lowry, and Ronan O'Gara, all of which contributed to a game-changing amount of funding for pancreatic trials. Last year Cancer Trials Ireland was unable to fund two trials in pancreatic cancer, so it is exciting to see this situation so dramatically reversed – and I look forward to the discussion of the Gastro-Intestinal DSSG around how this funding might be used!

I want to thank all staff for their support, Horse Racing Ireland for their own efforts, and finally, once again, Pat Smullen himself. We are committed to showing you the positive impact of your support as soon as we can.

While the Champions Weekend was a once in a lifetime event, Cancer Trials Ireland is also now the beneficiary of ongoing fundraising from new sources. In November 2018, the newly-formed Friends of Cancer Trials Ireland held a charity lunch to raise money to support efforts across Oesophageal, Lymphoma, Haematology, Lung, Gynaecological and Melanoma trials. For this we are indebted to volunteers and friends of Cancer Trials Ireland, who together helped raise €120,000 for Cancer Trials Ireland.

Other news

In other Group Central Office (GCO) news, much of our recent time in the GCO has been taken up with the HRB Review, ahead of our next grant cycle (commencing January 2021), and also with a recent HPRA inspection (October 2019). I want to thank all staff for their dedication through both of these intensive processes.

Finally I want to thank our outgoing Clinical Lead, Bryan Hennessy for all the work he has done for Cancer Trials Ireland over the past four years, including the help that he personally has given me. My tenure as CEO began at the same time as Bryan's time as the Clinical Lead, and I am glad that he will remain on as Vice-Clinical Lead for 2020 as Ray McDermott steps into the Clinical Lead role, and we begin the search for a new Vice-Clinical Lead to take that role in 2021.

Pat Smullen with AP McCoy (winning jockey)

Friends of Cancer Trials Ireland 2019

The second Friends of Cancer Trials Ireland lunch will take place on November 16th 2019 in Dublin. This year all funds raised will be put towards ovarian and prostate cancer trials. Pictured at last year's inaugural lunch: (Far right): Professor Ray McDermott, Grace McDermott. (Near right): Mary Fitzgerald, Maureen Carolan and Orla Holohan.

The Lithium Autophagy (CTRIAL-IE 11-32) trial opens in Ireland

Andrés Hernando, MSc, Senior Clinical Project Manager, Cancer Trials Ireland, Dublin, Ireland, Prof Seamus O'Reilly, Cork University Hospital, Ireland.

Sponsored by Cancer Trials Ireland, the Lithium Autophagy (CTRIAL-IE (ICORG) 11-32) trial is a phase Ib trial that will assess the addition of lithium to standard chemotherapy regimen of oxaliplatin and capecitabine to increase the activity of this regimen in patients with advanced, unresectable, oesophago-gastric or colorectal cancer who have received no previous treatment for advanced disease (previous adjuvant or neo-adjuvant treatment is acceptable if completed at least 6 months prior to registration).

Previously completed studies at University College Cork have demonstrated enhanced antitumor activity when lithium is combined with platinum based chemotherapy in in vitro and in vivo systems. This has led to the current Phase I trial.

This is a phase Ib open label, multi-centre trial of lithium in combination with oxaliplatin and capecitabine. Eligible patients will receive oxaliplatin at 130mg/m^2 i.v. on day 1 of a 21-day cycle and capecitabine 1,000mg/m^2 b.i.d. p.o. on days 1 to 14 of each 3-week cycle plus lithium. There will be 4 different dose levels of lithium according to the dose escalation scheme (dose level 1: 0.6mmol/l [target concentration], dose level 2: 0.9mmol/l [target concentration], dose level 3: 1.26mmol/l [target concentration], dose level 4: 1.4mmol/l [target concentration]) to determine the maximum tolerated dose (MTD) based on the occurrence of dose limiting toxicity (DLT). There will be a dose level -1 (0.4mmol/l [target concentration]) in case dose de-escalation is needed. We will enrol 3 to 6 patients per dose level according to a traditional 3+3 design, with dose escalation and determination of MTD based on the occurrence of DLT, using the usual threshold probability of 33%. All patients in each level must have completed at least two cycles of therapy before enrolment in the next dose level. Patients not completing two cycles for a reason other than toxicity will be replaced.

Although the main endpoint of this trial is safety, efficacy measures (such as progression free survival (PFS), objective response rate (ORR) and overall survival (OS)) will also be evaluated in patients treated with this regimen. The trial has translational sub-studies (exploratory objectives) to examine predictive biomarkers in tumour tissue and pleural effusion and/or ascites samples.

This trial is a national study that will run in 2 sites in Ireland. The trial was recently initiated in *Cork University Hospital* and it is planned to enrol the first patient in November 2019. Maximum of 24 patients will be enrolled in the trial. The number of patients enrolled will be determined by the number of patient cohorts which are required to estimate the MTD during the dose escalation.

We hypothesize that the addition of lithium to cytotoxic chemotherapy will increase the activity of the regimen and that the lack of significant overlapping toxicities will not compromise tolerability.

Trial Chief Investigator Professor Seamus O'Reilly (top left) and Andrés Hernando, MSc, Senior Clinical Project Manager

RsqVD trial update

The RsqVD trial (Chief Investigator is Professor Peter O'Gorman at the Mater Misericordiae University Hospital) will have all patient visits completed by the end of October 2019. Forty two patients were enrolled in this Phase II Study evaluating the Efficacy and Safety of lenalidomide, subcutaneous bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma across 8 investigator sites nationwide.

A recent protocol amendment allowed for patients to end maintenance treatment on the study and continue on treatment as standard of care going forward. Patients may continue to be followed for overall survival in this study through National Cancer Registry Ireland.

A huge effort has been made in recent months on the part of the trial sites and the Cancer Trials Ireland study team to ensure that data is clean for a manuscript on overall response rate after 4 cycles of induction therapy which is the primary endpoint for this study. Thanks to everyone for their support!

Picture: Members of the Cancer Trials Ireland Data Management and Clinical Monitoring Teams for RsqVD (left to right: Lucy Short (CDM), Marc Nolan (Senior CDM), Leela O'Shea (CRA), Roisin Keogh (SCRA)

Panthera (CTRIAL 17-13), PantHER sister trial, opens in Ireland

Andrés Hernando, MSc, Senior Clinical Project Manager, Cancer Trials Ireland, Dublin, Ireland, Prof Bryan T Hennessy, Clinical Lead, Cancer Trials Ireland, RCSI Molecular Medicine and Beaumont Hospital, Dublin, Ireland.

Sponsored by Cancer Trials Ireland, the Panthera (CTRIAL-IE 17-13) trial is a phase Ib trial that will assess the addition of copanlisib to T-DM1 (trastuzumab emtansine) to overcome HER2-therapy resistance in patients with unresectable locally advanced or metastatic HER2-positive breast cancer who previously received trastuzumab and a taxane, separately or in combination.

This is a phase Ib open label, single arm adaptive, multi-centre trial of copanlisib in combination with T-DM1. Eligible patients will receive T-DM1 at 3.6mg/kg i.v. on day 1 of a 21-day cycle plus copanlisib. There will be 3 different dose levels of copanlisib according to the dose escalation scheme (dose level 1: 45mg on days 1 and 8, dose level 2: 60mg on days 1 and 8, dose level 3: 60mg on days 1, 8, and 15) to determine the maximum tolerated dose (MTD) based on the occurrence of dose limiting toxicity (DLT). There will be a dose level -1 (45mg on day 1 only) in case dose de-escalation is needed. We will enrol 3 to 6 patients per dose level according to a standard 3+3 algorithm, with dose escalation and determination of MTD based on the occurrence of DLT, using the usual threshold probability of 33%. The final dose level will be expanded to include a total of 6 additional patients (expansion cohort). All patients in each level must have completed at least the first cycle of therapy before enrolment in the next dose level. Patients not completing the first cycle for a reason other than toxicity will be replaced.

Although the main endpoint of this trial is safety, efficacy measures (such as progression free survival (PFS), time to failure (TTF), duration of response (DR) and overall survival (OS)) will also be evaluated in patients treated with this regimen. The trial has translational sub-studies (exploratory objectives) to examine predictive biomarkers in tumour tissue and blood as well as molecular tumour adaptation to clinical trial therapy

This trial is a binational study that will run in 3 sites in Ireland (*Beaumont Hospital*, *Cork University Hospital* and *St Vincent's University Hospital*) and one site in Spain. The trial was initiated in Ireland in September 2019 and it is planned to enrol the first patient in November 2019. Maximum of 24 patients with either wild or mutant PI3KCA will be enrolled in the trial.

Breast cancer (BC) is the second most common cancer and the fifth cause of cancer mortality worldwide[1]. Approximately 20% of cases of breast cancer overexpress the Human Epidermal Growth Factor Receptor (HER2), and HER2-positivity is associated with a significantly worse prognosis. HER2 was first targeted by trastuzumab which significantly improved outcomes, but the efficacy of trastuzumab is limited by acquired and de novo resistance[2].

The phosphoinositide 3 kinase (PI3K) pathway is important in the oncogenic function of HER2[3]. Aberrant activation of PI3K is implicated in resistance to trastuzumab and other HER2-targeted therapies[4] and is frequent, with up to 22% of HER2 positive BC having a PIK3CA mutation[5]. Copanlisib is a pan-class 1 PI3K inhibitor administered intravenously, with low nanomolar activity against both PI3Kα and PI3Kβ. Copanlisib has been shown to re-sensitise trastuzumab resistant cell lines to trastuzumab with synergism seen in some cell lines between copanlisib and HER2 targeted therapy[6].

Addition of a PI3K inhibitor to anti-HER2 therapy is a potential hope to improve outcomes in HER2-positive advanced breast cancer.

References:

1. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012., 2012
2. Berns K, Horlings HM, Hennessy BT, et al. A functional genetic approach identifies the PI3K pathway as a major determinant of trastuzumab resistance in breast cancer. Cancer Cell. 2007;12: 395-402.
3. Yakes, F.M. et al Cancer research, 2002;62(14), pp.4132-4141.
4. Berns, K.et al Cancer cell, 2007;12(4), pp.395-402.
5. Stemke-Hale, K.et al Cancer research, 2008;68(15), pp. 6084-6091.
6. Elster, N.et al Breast cancer research and treatment, 2015;149(2), pp.373-383.

Professor Bryan Hennessy, Clinical Lead, Cancer Trials Ireland, RCSI Molecular Medicine and Beaumont Hospital, Dublin, Ireland.

New Prostate Cancer Registry Study opens in Ireland: IRONMAN (CTRIAL-IE 17 -30) An International Registry for Men with Advanced Prostate Cancer

Dr Anne-Marie Byrne, PhD, Trial Coordinator, Dr Orla Casey, PhD, Translational Project Manager, Cancer Trials Ireland, Prof Ray McDermott, Chief Investigator, Beacon Hospital, Tallaght University Hospital and St Vincent's University Hospital, Dublin, Ireland.

Cancer Trials Ireland has opened a Prostate Cancer Registry study for men with advanced prostate cancer in conjunction with the study sponsor, the Prostate Cancer Clinical Trial Consortium (PCCTC). The study is funded by the Movember Foundation.

Each year more than 3000 men are diagnosed with prostate cancer in Ireland and over 300 men die from this disease. There are many new treatments and therapies available for prostate cancer, but we don't understand which treatments and care practices deliver the best outcomes for men with advanced prostate cancer.

The IRONMAN registry collects information about a man's type of prostate cancer, their treatment and any side effects they may be experiencing. Collecting and researching this information will enable us to better understand what causes prostate cancer, how to stop or slow its progression, and how to provide the best possible care to enable men to live the best quality life possible.

The study seeks to improve the lives of men with advanced prostate cancer by (i) Identifying which treatments or combinations of treatments are associated with the highest rates of survival and quality of life, (ii) determining if treatments are associated with side effects and other diseases or conditions, (iii) developing a collection of blood samples to allow research on different types of prostate cancer and (iv) creating an international partnership to work together and identify the unmet needs of men with advanced prostate cancer.

The IRONMAN study is open in 10 countries and will recruit 5000 men in a global effort to identify best treatment practices and strategies for men with advanced prostate cancer. By collecting this information, we will understand which treatment and care practices deliver the best outcomes for prostate cancer patients. This information will be shared across the globe, so that all men can benefit from this knowledge.

The study will open in several Irish sites and recruit 300 men with advanced prostate cancer. The Chief Investigator is Prof Ray McDermott. The study opened in Ireland at the Beacon Hospital in July 2019. The study is also open in St Vincent's University Hospital who recruited the first patient. The study has been initiated and due to open soon in Tallaght University Hospital and will also open in Cork University Hospital, University Hospital Limerick, Sligo University Hospital, Mater Misericordiae University Hospital and the Mater Private hospital. Further information can be found on https://ironmanregistry.org/, www.cancertrials.ie and https://clinicaltrials.gov/ (ID: NCT03151629).

IRONMAN Registry study opened in The Beacon Hospital July 2019. Pictured above-Chief investigator for the study Prof Ray McDermott and Sub-Investigator Dr Alina Mihai of the Beacon Hospital.

First Person Recruited to the COLOSSUS (CTRIAL-IE 17-26) Study in Ireland

Dr Magdalena Mroz, PhD, Clinical Research Associate, Dr Orla Casey, PhD, Translational Project Manager, Cancer Trials Ireland, Prof Ray McDermott, Chief Investigator, Tallaght University Hospital and St Vincent's University Hospital, Dublin, Ireland.

Dr Brian Bird and his team at the Bon Secours Hospital in Cork have recently enrolled the first person in Ireland to the COLOSSUS translational trial.

COLOSSUS is an EU-funded Horizon 2020 project that aims to provide new and more effective ways to classify people with a specific subtype of metastatic colorectal cancer, MSS RAS mt mCRC (microsatellite stable RAS mutant metastatic colorectal cancer). Current treatment for MSS RAS mt mCRC is primarily based on 5-fluorouracil based chemotherapy +/- bevacizumab. However, there are limited treatment options for patients with this type of cancer when they develop resistance to standard treatment.

The COLOSSUS project and translational trial collects and analyses blood and colon tumour samples and applies advanced multi-omic computational modelling approaches to identify new MSS RAS mt specific subtypes. This strategy is designed to help predict patient outcomes under standard treatment and to enable the design of more targeted and personalised regimens.

The ultimate project goal is to deliver a personalised medicine approach for patients with MSS RAS mt mCRC. Watch our short explainer video here.

The COLOSSUS trial is open now in hospitals across Ireland, Spain and Germany. Read more about the trial criteria, who to contact and how to get involved here.

The COLOSSUS project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 754923. The material presented and views expressed here are the responsibility of the author(s) only. The EU Commission takes no responsibility for any use made of the information set out.

An ovarian cancer feasibility study open to assess a new BRCA1/2 mutation testing pathway in the oncology clinic: The tBRCA Study (CTRIAL-IE 18-01)

Dr Anne-Marie Byrne, PhD, Trial Coordinator, Dr Orla Casey, PhD, Translational Project Manager, Cancer Trials Ireland, Prof Bryan T Hennessy, Clinical Lead, Cancer Trials Ireland & Chief Investigator, Dr Roshni Kalachand, Co-Investigator, RCSI Molecular Medicine and Beaumont Hospital, Dublin, Ireland.

Cancer Trials Ireland opened a translational study: "CTRIAL-IE 18 -01: Upfront systematic tumour BRCA testing in patients with high grade serous or endometrioid ovarian, fallopian tube or primary peritoneal cancer (HGSEC) -**The tBRCA Study."**

It is important to identify if ovarian cancer is due to a germline or somatic BRCA1/2 mutation because it provides information that can help guide treatment, informs the patient about future risk of developing cancer and informs the patient about risk for their relatives of developing cancer.

All patients with high grade serous or endometroid ovarian, fallopian tube or primary peritoneal cancer (HGSEC), either at primary diagnosis or first relapse, are eligible for this study. The total number of patients to be enrolled is 200.

This study aims to assess the feasibility and potential resource impact of the initiation of an upfront routine ovarian cancer tumour tissue BRCA1/2 mutation testing pathway in the oncology clinic in terms of clinicians' and patients' experience, impact on patient management and health-economic analysis.

This study will also determine the rates, patterns and types of BRCA1/2 mutations in HGSEC in Ireland, and identify the patient characteristics, disease course, treatment patterns and clinical outcomes associated with BRCA1/2-mutated HGSEC, as compared to BRCA1/2 wild type disease.

Cancer Trials Ireland is the sponsor for this study, with Prof Bryan Hennessy as Chief Investigator and Dr Roshni Kalachand (RCSI) as the Co-Investigator. The tBRCA Study was opened in University Hospital Limerick (Dr Grzegorz Korpanty) in March 2019 where the first patient was recruited. The study has since been opened in the Bon Secours Cork (Dr Conleth Murphy), Cork University Hospital (Dr Dearbhaile Collins), Mater Misericordiae University Hospital & Mater Private hospital (Prof Cathy Kelly) and St James's Hospital (Mr Feras Abu Saadeh). The study is also due to open soon in University Hospital Waterford (Dr Paula Calvert). Recruitment is going very well with 65 patients on study to date.

St James's Hospital - PI Mr Feras Abu Saadeh and the team

Academic publications from Cancer Trials Ireland Investigators

Dr Orla Casey, Translational Project Manager, Cancer Trials Ireland

Breast

Cancer Trials Ireland Study Number: short name. 01-04: BCIRG 005

Press, M. F., J. A. Seoane, C. Curtis, E. Quinaux, R. Guzman, G. Sauter, W. Eiermann, J. R. Mackey, N. Robert, T. Pienkowski, J. Crown, M. Martin, V. Valero, V. Bee, Y. Ma, I. Villalobos and D. J. Slamon (2019). "**Assessment of ERBB2/HER2 Status in HER2-Equivocal Breast Cancers by FISH and 2013/2014 ASCO-CAP Guidelines.**" JAMA Oncol **5**(3): 366-375.

Cancer Trials Ireland Study Number: short name. 08-10: TC-Avastin

Gullo, G., A. J Eustace, A. Canonici, D. M Collins, M. J. Kennedy, L. Grogan, O. Breathhnach, J. McCaffrey, M. Keane, M. J. Martin, R. Gupta, G. Leonard, M. O'Connor, P. M. Calvert, P. Donnellan, J. Walshe, E. McDermott, K. Scott, A. Hernando, I. Parker, D. W Murray, A. C O'Farrell, A. Maratha, P. Dicker, M. Rafferty, V. Murphy, N. O'Donovan, W. M Gallagher, B. Ky, D. Tryfonopoulos, B. Moulton, A. T Byrne and J. Crown (2019). "**Pilot study of bevacizumab in combination with docetaxel and cyclophosphamide as adjuvant treatment for patients with early stage HER-2 negative breast cancer, including analysis of candidate circulating markers of cardiac toxicity: ICORG 08-10 trial.**" Ther Adv Med Oncol **11**: 1758835919864236.

Gastrointestinal

Cancer Trials Ireland Study Number: short name. 12-38: TRI-LARC

Brennan, V. S., B. Curran, C. Skourou, E. McVeigh, M. Dunne, L. O'Sullivan and B. D. P. O'Neill (2019). "**A novel dynamic arc treatment planning solution to reduce dose to small bowel in preoperative radiotherapy for rectal cancer.**" Med Dosim **44**(3): 258-265.

Genitourinary

Cancer Trials Ireland Study Number: short name. 08-17: IMRT Prostate

Medipally, D. K. R., T. N. Q. Nguyen, J. Bryant, V. Untereiner, G. D. Sockalingum, D. Cullen, E. Noone, S. Bradshaw, M. Finn, M. Dunne, A. M. Shannon, J. Armstrong, F. M. Lyng and A. D. Meade (2019). "**Monitoring Radiotherapeutic Response in Prostate Cancer Patients Using High Throughput FTIR Spectroscopy of Liquid Biopsies**." Cancers (Basel) **11**(7).

Cancer Trials Ireland Study Number: short name. 14-06: ANZUP ENZAMET Study

Davis, I. D., A. J. Martin, M. R. Stockler, S. Begbie, K. N. Chi, S. Chowdhury, X. Coskinas, M. Frydenberg, W. E. Hague, L. G. Horvath, A. M. Joshua, N. J. Lawrence, G. Marx, J. McCaffrey, R. McDermott, M. McJannett, S. A. North, F. Parnis, W. Parulekar, D. W. Pook, M. N. Reaume, S. K. Sandhu, A. Tan, T. H. Tan, A. Thomson, E. Tu, F. Vera-Badillo, S. G. Williams, S. Yip, A. Y. Zhang, R. R. Zielinski, C. J. Sweeney and E. T. I. a. t. A. a. N. Z. U. a. P. C. T. Group (2019). "**Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer.**" N Engl J Med **381**(2): 121-131.

Lymphoma and Haematology

Cancer Trials Ireland Study Number: short name. 15-10: OPTIMISMM

Richardson, P. G., A. Oriol, M. Beksac, A. M. Liberati, M. Galli, F. Schjesvold, J. Lindsay, K. Weisel, D. White, T. Facon, J. San Miguel, K. Sunami, P. O'Gorman, P. Sonneveld, P. Robak, S. Semochkin, S. Schey, X. Yu, T. Doerr, A. Bensmaine, T. Biyukov, T. Peluso, M. Zaki, K. Anderson, M. Dimopoulos and O. t. investigators (2019). "**Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial.**" Lancet Oncol **20**(6): 781-794.

Cancer Trials Ireland Study Number: short name. 16-02: CyBorD-DARA

O'Dwyer, M., R. Henderson, S. D. Naicker, M. R. Cahill, P. Murphy, V. Mykytiv, J. Quinn, C. McEllistrim, J. Krawczyk, J. Walsh, E. Lenihan, T. Kenny, A. Hernando, G. Hirakata, I. Parker, E. Kinsella, G. Gannon, A. Natoni, K. Lynch and A. E. Ryan (2019). "**CyBorD-DARA is potent initial induction for MM and enhances ADCP: initial results of the 16-BCNI-001/CTRIAL-IE 16-02 study.**" Blood Adv **3**(12): 1815-1825.

Cancer Trials Ireland studies open to accrual

Purple = Industry studies Green = Cancer Trials Ireland studies Orange = Collaborative Group studies

DSSG	General Group	Cancer Trials Ireland No:	Study Name:	Total Accrual	TUH	Beacon	BH	BonS
Breast	Trans	09-07	Breast Cancer Proteomics and Molecular Heterogeneity	2689			1295	
Breast	Trans	10-11	Circulating miRNA	253			33	20
Breast	Trans	15-34	Recurrence Score	83			15	
Breast	Clinical	15-02	PantHER	15			9	
Breast	Radio	15-03	NSABP B-51	18				
Breast	Clinical	16-20	POSITIVE	13				
Breast	Clinical	17-15	IMpassion030/ALEXANDRA	6			4	
Breast	Clinical	17-33	VIOLETTE	5				
Breast	Clinical	18-05	KEYNOTE-756	3				Open
Breast	Clinical	18-41	NATALEE	4			Open	
CNS	Trans	08-13	Serum Protein Markers for Glioma	146			146	
CNS	Radio	15-41	ROAM	1				
GI	Clinical	10-14	Neo-AEGIS	347			1	
GI	Clinical	11-32	Lithium	0				
GI	Trans	12-27	CRAC Plasma Biomarkers	109	3	Open	38	21
GI	Trans	12-31	PDAC Plasma Biomarkers	160	41	Open	17	27
GI	Radio	12-38	TRI-LARC	82				
GI	Trans	17-26	COLOSSUS	3	Open			1
GI	Clincal	18-12	MK 3475-811	3	1		2	
GI	Clincal	18-30	MK3475-859	2	1		1	
GI	Clincal	18-43	MK 7902-002	0				
GI	Clincal	19-07	MK3475-937	0	opening soon			
GI	Clincal	19-08	SOLSTICE	1	Open			Open
GU	Clinical	11-34	TIGER	2				
GU	Clinical	13-23	Neo-adjuvant Abiraterone prostate	41				
GU	Clinical	16-21	PEACE III	0	Open			
GU	Clinical	16-63	Roche IMmotion010	11	5			
GU	Clinical	16-69	Eisai E7080-G000-307	16	8		5	
GU	Clinical	16-70	BMS CA209-274	12	8			
GU	Clinical	17-03	Roche CO39303	12	7			
GU	Clinical	17-04	Bayer 17403/ FORT-1	6	3			
GU	Clinical	17-17	DICE	7	3			
GU	Trans	17-30	IRONMAN	2	TBI	Open		
GU	Radio	18-02	NRG GU005	7		7		
GU	Clinical	18-31	Keynote-564	1	Initiated			
Gynae	Radio	09-06	Endometrial - IMRT v 3D RT	89				
Gynae	Clinical	11-29	ICON8B	31				3
Gynae	Clinical	14-02	SHAPE	14				
Gynae	Trans	18-01	tBRCA Study	63				5
Gynae	Radio	18-27	PORTEC-4a	1				
Gynae	Clinical	19-09	MK3475-775	3				

Open Studies | Studies To Be Initiated | Studies Pending

CUH	UHG	LUH	Mater	MRH	MUH	OLLHD	OLCHC	UHL	SLRON	SJH	SUH	SVUH	UHW	Whit	International Sites
677								385		Open		Open	332		
	134			15		1				30	18	Open	2		
16	6	3	1					10		11		12	9		
2	Open									Open		4			
	6								12						
	2							2		1		8	Open		
			2					Open							
2	Open											3			
										3					
Open			Open					1		Open		3	Open		
									1						
7	1								Open	117					221
Open															
-	13	3	3			2				Open	14	2	10		
-	3	TBI										65	7		
									82						
	Open											TBI			2
										Open					
										Open					
			Open									Open			
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1															
										2					
24	3								14						
TBI									TBI			TBI			
6															
2	1														
4															
1			4												
3										TBI					
2	TBI							1			TBI	0	1		
												2			
									Pend						
												1	Initiated		
									89						
	5		14							0			9		
										14					
Open			26					8		24			TBI		
									1						
			3												

Cancer Trials Ireland studies open to accrual

Purple = Industry studies Green = Cancer Trials Ireland studies Orange = Collaborative Group studies

DSSG	General Group	Cancer Trials Ireland No:	Study Name:	Total Accrual	TUH	Beacon	BH	Bon's
Gynae	Clinical	18-35	ENGOT CX8	1				
Gynae	Clinical	18-26	Athena	2				
H&L	Clinical	18-48	CALLS (INCB 84344-401)	0			TBI	
H&L	Clinical	18-15	Paradigme	1				
H & L	Clinical	15-38	CHRONOS-3	5			Closed	
H & L	Clinical	15-36	Protocol 04-30 (INSPIRE)	3	1			
H & L	Clinical	16-60	CLL13	38			6	
H & L	Clinical	17-06	CHRONOS 4	2				
H & L	Clinical	17-07	CheckMate 744	1				
Lung	Radio	15-47	INTENSE	6		TBI		
Lung	Clinical	15-40	MK3475-091 (PEARLS)	26				
Lung	Clinical	16-25	Roche MO29872 (closed to accrual 24-Jul-2019)	4				
Lung	Clinical	16-80	Abbvie Meru M16-298 (closed to accrual 12-Jul-2019)	8			Closed	
Lung	Clinical	16-59	ALERT-Lung	0				
Lung	Clinical	17-09	MK3475-598 (closed to accrual 19-Jul-2019)	7			2	
Lung	Clinical	17-34	MK3475-495	0				
Lung	Cinical	17-37	MK3475-671	0				
Lung	Clinical	18-14	EMPOWER 16113 (closed to accrual 20-Mar-2019)	2			1	
Lung	Clinical	18-49	AbbVie M14-239	0				
Basket	Trans	08-40	SNP Study	161	17		11	40
Basket	Clinical	15-42	LOXO-101	5				
Basket	Clinical	16-19	Add-Aspirin	48	4		3	4
Paeds	Trans	16-34	LLR Leukaemia Cell bank	32				
Paeds	Trans	16-37	EWOG-MDS-2006	1				
Paeds	Clinical	16-39	LTI Study	0				
Paeds	Clinical	16-40	NBL BEACON	1				
Paeds	Clinical	16-41	LINES	0				
Paeds	Trans	16-42	IMPORT	4				
Paeds	Trans	16-43	Tumour Banking Study	25				
Paeds	Registry	16-44	EU-Rhabdoid Registry	1				
Paeds	Trans	16-46	EWOG-SAA 2010	1				
Paeds	Clinical	16-52	EURO EWING 2012	1				
Paeds	Clinical	16-53	Interfant 06	2				
Paeds	Clinical	18-19	MAPPYACTS	4				
Paeds	Clinical	18-22	CHIMERIX ADAPT*	3				
Paeds	Clinical	16-82	Mye Child	2				
Paeds	Clinical	18-17	PHITT	3				
Paeds	Clinical	18-36	LOXO TRK 15003	1				
Paeds	Trans	19-04	Monte BM study	3				
Paeds	Trans	19-05	NBL NK study	1				

Open Studies | Studies To Be Initiated | Studies Pending

CUH	UHG	LUH	Mater	MRH	MUH	OLLHD	OLCHC	UHL	SLRON	SJH	SUH	SVUH	UHW	Whit	International Sites
1															
1								1							
TBI			TBI					TBI		TBI		TBI	Open		
	Open		Open							1					
	2		0							3		Open			
1	Closed												1		
7	6		5							9			5		
2			Open							Closed					
							On hold			1					
									6						
6			3					5		11			1		
			3					1							
3										1		4	0		
										Open					
								1		4					
								Open		Open					
								Open		TBI					
								1							
TBI										TBI		TBI			
1	26		2								26	Pend	38		
												5			
5	3		3					14	Open		7	Open	5		
							32								
							1								
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							1								

Annual Report 2018

Chairman's message

Dr. Jonathan Westrup

In 2018, Cancer Trials Ireland took on the challenge to transform our decision making around adding new trials to our portfolio. We also worked with key stakeholders to investigate ways to contribute to the targets set by the National Cancer Strategy (2017). We met with the Department of Health, Health Research Board, NCCP and InterTrade Ireland to progress ideas on how to double the number of patients on clinical trials in Ireland. We are not there yet, but we have built a shared vision for enhancing clinical trials capability at our hospital cancer units.

Following on from the success of Cancer Trials Ireland 2017 Strategy Day, the Leadership Team and Board of Directors spent a day in early 2018 planning for the future, formulating an implementation plan based on the Strategy Report 'Towards 2020'. The strategy continues to underpin the organisation's direction through challenging times and supported the development of new processes and functions in the General Central Office (GCO). Actions were also informed by outcomes from regulatory inspections and a review of technical accounting practices in order to make optimal use of funds available.

The 20% funding cut to the HRB Grant (2016-18) resulted in the organisation coming under considerable financial pressure in 2018 and decisions had to be made of what we could and could not do going forward. The Board sought the support of our Clinical Executive and Scientific Management Committee and had to make tough calls. We reduced the number of new in-house trials we could open and financially support. Trials which were well funded by collaborative groups and industry were more achievable for us in this period. We know that colleagues at our hospital sites 2018 had to make similar calls on trials.

While the trial numbers are positive and the portfolio is balanced between disease types, a deeper dive shows a reduction in the number of new in-house academic trials and an increase in collaborative group and industry-funded Investigator Initiated Trials. This growth is good for patients but we could do better.

The Board acknowledges that Cancer Trials Ireland need to have the ability to resource more in-house academic trials. I am happy to report in 2019 our funding model is evolving and through initiatives like the Friends of Cancer Trials Ireland and the Pat Smullen Fund, we can now look at opening more academic-led trials targeting gaps in our portfolio and thereby bringing more options to Irish patients.

Finally, I want to thank my colleagues on the Board for their steadfast commitment to Cancer Trials Ireland. The Board are very proud of the research that is driven by the clinical members of this group working hard in our cancer units and the staff at GCO, all making a difference to cancer patients lives.

Vision & Mission

The Board rotates at the AGM every year as per the Constitution. The Board is chaired by Dr. Jonathan Westrup, appointed in 2014 and he is a strategy and governance expert. The Board meets 5 times per year and permanent agenda items include reports from Clinical Executive Committee and Audit Committee

The vision at Cancer Trials Ireland is focused on one primary purpose. To provide every patient with cancer access to high-quality and potentially life altering cancer trials and make Ireland a highly attractive location to open cancer trials. Our mission is to discover new diagnostics and treatments that will extend and enhance the lives of the millions of people who are diagnosed with cancer each year.

In order to achieve this vision, Cancer Trials Ireland must undertake translational and clinical cancer trials which investigate all disease areas and it must have in place the organisational capability to do so.

The 5 strategic pillars are the key to enable Cancer Trials Ireland to achieve this vision and mission:

1. **Governance**
2. **Profile**
3. **Funding Model**
4. **Operational Capabilities**
5. **Clinical Capabilities**

What we do

Since Cancer Trials Ireland was established in 1996, more than 15,000 patients have participated in over 350 of its trials. Almost all cancer treating specialists in Ireland are members of Cancer Trials Ireland.

The trials are carried out in 14 hospital-based Cancer Trials Units (CTUs) across the country that are supported by a central team of clinical researchers, project managers, data managers and other experts. As well as managing its own in-house academic trials, Cancer Trials Ireland also works with global pharmaceutical companies and international collaborative research groups from around the world which generates substantial inward investment and access to innovative treatments for cancer patients.

During 2018, in the 14 hospital-based research units, Cancer Trials Ireland were working on 81 trials actively recruiting patients and involving approximately 6,000 patients with an additional 4,000 patients enrolled onto patient registry studies. All these trials involved the staff at Cancer Trials Ireland General Central Office.

In 2018, approximately, 20% of the trials are in-house academic trials (2017: 20%) funded by the grants received from the Health Research Board and the Irish Cancer Society. The other 41% (2017: 34%) of these trials involved collaboration with cancer research groups and/or Investigator Initiated Studies which are funded through pharmaceutical companies. 39% (2017: 46%) of trials on our portfolio are trials run by international pharmaceutical companies in Irish hospitals where staff at the General Central Office do limited work and receive no support. However, for a complete picture we adopt them to our portfolio.

Achievements & Performance 2018

- The Health Research Board conducted an external scientific panel review of the work of Cancer Trials Ireland in 2018. The report from the panel was very positive about the work of the group and has informed the decision to award a 4-year grant (2021-24) including moving the Data and Statistics function to Cancer Trials Ireland. The award will be subject to the usual considerations.
- Cancer Trials Ireland ran the third successful externally funded Just Ask Your Doctor public information campaign communicating with the public and members on radio and media interviews on the value of cancer trials.
- Cancer Trials Ireland advocacy activities in 2018 included making representations to the Department of Health, NCCP and the Minister for Health's office;
- A group of volunteers came together to offer their support to Cancer Trials Ireland and an inaugural lunch to raise awareness and funds to help Cancer Trials Ireland's important work was held. Patients who took part in some of our trials were represented by friends and family and were the biggest supporters at the event. The success of the event is an incredible testament to the work of the team at Cancer Trials Ireland.
- Cancer Trials Ireland facilitated regular Stakeholder Engagement and Patient Advocate Advisory Group (PAAG) meetings in 2018 including working with partners in the Northern Ireland Cancer Trials Network on sharing ideas on trials and exchanging learnings on patient involvement in research.

Pictured (L to R) Dr Jerome Coffey, Director of the NCCP; Simon Harris TD, Minister for Health; Prof Bryan Hennessy, Clinical Lead; Dr Linda Coate, Vice Clinical Lead; and Eibhlin Mulroe, CEO.

(L to R) Ann Marie Cullen, Head of Oncology Medical Affairs, Novartis; Orlaith Gavan, Oncology Medical Lead, Pfizer; Paula Moyles & Mairead Henderson, Country Study Managers, Roche; Prof Bryan Hennessy, Clinical Lead, Cancer Trials Ireland; Ashlin Dunne, Regional Project Management Lead – Oncology, MSD; Eibhlín Mulroe, CEO, Cancer Trials Ireland; Dr Linda Coate, Vice Clinical Lead, Cancer Trials Ireland; Dr Jonathan Westrup, Chair, Cancer Trials Ireland; Evelyn O'Rourke, Board of Cancer Trials Ireland; Dr Paul Kelly, Consultant Radiation Oncologist, Cork University Hospital; Dr Robert O'Connor, Head of Research, Irish Cancer Society, both on Board of Cancer Trials Ireland.

Structure, governance & management

The Board rotates at the AGM every year as per the Constitution. The Board is chaired by Dr. Jonathan Westrup, appointed in 2014 and he is a strategy and governance expert. The Board meets 5 times per year and permanent agenda items include reports from Clinical Executive Committee and Audit Committee, Governance, Strategy, Conflict of Interest Declarations and Finance. In 2018, the Board met 5 times and had 2 additional special Board meetings. The Board met 5 times in 2017. (2017: 5)

The members of the Board are qualified to hold their position and represent a range of skills; governance, patient advocate, clinical oncologists, radiation oncologists, industry representative, finance and National Cancer and Control Programme (NCCP) representative. In 2018 the Board appointed a new subgroup called the Patient Consultant's Committee (PCC) set up to integrate the patient voice and experience in the governance structure of the organization. Diane Hanly is the Chair of the PCC and was elected to the Board at the AGM in 2018.

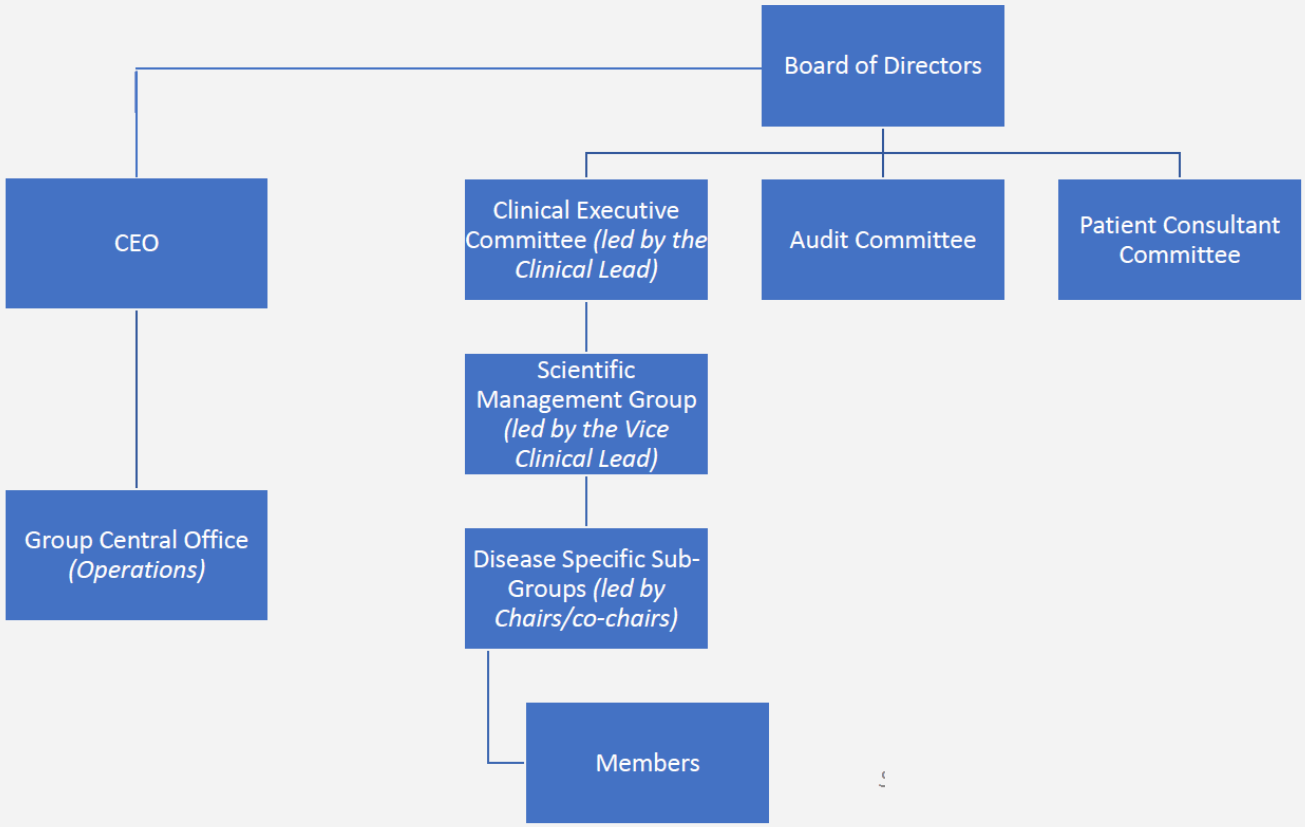
The Clinical Executive Committee (CEC), Scientific Management Group and Disease Specific SubGroups monitor progress on the ongoing clinical trials, make decisions on the adoption of new trials to the portfolio and the CEC reports to the Board of Directors through its Chair; Prof. Bryan Hennessy, Clinical Lead.

The Audit Committee is a subcommittee of the Board and was established in the summer of 2016 and met 3 times in 2018 (2017:4) Darren Byrne is the chair of the Audit Committee and member of the Board of Directors.

Directors:

- Dr. Jonathan Westrup (Chairman)
- Darren Byrne
- Dr. Linda Coate (Appointed 17th May 2018)
- Dr. Jerome Coffey
- Dr. Leisha Daly
- Berchmans Gannon
- Diane Hanly (appointed 8th November 2018)
- Prof. Bryan Hennessy
- Dr. Cathy Kelly (Resigned 17th May 2018)
- Dr. Paul Kelly
- Prof. Ray McDermott
- Prof. Patrick Murray (Resigned 17th May 2018)
- Dr. Robert O'Connor
- Evelyn O'Rourke;

Secretary: Mr. Robert Cosgrave



Statement of income & retained earnings for the financial year ended 31 December 2018

	2018	2017
	€	€
Income	3,543, 126	3,570,106
Expenditure	-3,442,452	-3,948,115
Surplus / (Deficit) on ordinary activities before interest)	100,674	-378,009
Interest receivable and similar income	4,198	9,815
SURPLUS/ (DEFICIT) FOR THE FINANCIAL YEAR	104,872	-368,194
RETAINED EARNINGS AT THE BEGINNING OF THE FINANCIAL YEAR	293,732	661,926
RETAINED EARNINGS AT THE END OFTHE FINANCIAL YEAR	398,604	293,732

Balance Sheet as at 31 December 2018

	2018	2017
	€	€
Fixed Assets		
Tangible assets	**14,183**	25,426
Current Assets		
Debtors	**1,463,076**	1,849,389
Cash and cash equivalents	**2,870,645**	2,917,040
	4,333,721	4,766,429
Creditors: Amounts falling due within one year	**-3,949,300**	-4,498,123
Net Current Assets	**384,421**	268,306
Net Assets	**398,604**	293,732
Reserves		
Retained earnings	**398,604**	293,732
	398,604	293,732

Berchmans Gannon
Director

Darren Byrne
Director

*Full copy of financial statements for 2018 at www.cancertrials.ie

We said goodbye to a special friend in April this year, when artist Ruth Larkin passed away. Ruth had breast cancer and she took part in three clinical trials in the course of her treatment. She was a tremendous advocate for clinical trials, and her participation in them went on to inspire her work as an artist. Ruth visited research facilities to inform an exhibition she was developing called 'The Vitruvian Man', which was based on Da Vinci's famous drawing of the same name. In her own words:

"I wish to make sense of the internal workings of my own body in the context of cancer treatments.. ..I have approached the changes in my cellular structure by exploring landscape, portraiture and science." Her aim was to develop a new method to interpret cellular information and the relationship between time and changing landscapes. Ruth's family recently staged an exhibition of Ruth's work since 1974 in the Temple Bar Gallery in October to honour her memory.

"The mind has the ability to reason, love and be creative."

Translational team pictures

1. The tBRCA study: University Hospital Limerick - PI Dr Grzegorz Korpanty and the team

2. The tBRCA study: Cork University Hospital - Principal Investigator Dr Dearbhaile Collins and the team

3. The tBRCA study: Mater Misericordiae Hospital & Mater Private hospital - Principal Investigator Dr Cathy Kelly and the team

4. The tBRCA and COLOSSUS studies: Bon Secours Hospital Cork **-** Principle Investigators Dr Conleth Murphy and Dr Brian Bird and the team

And finally:Thank you, Pat Smullen!

This event has raised the profile of our work and we know that more people than ever before are checking our website to see what cancer trials are available. There are patients today asking their doctors about trials because you raised awareness.

Thank you for helping us to bring more hope to more patients. The doctors, nurse and research staff of Cancer Trials Ireland are humbled by your generosity and support.