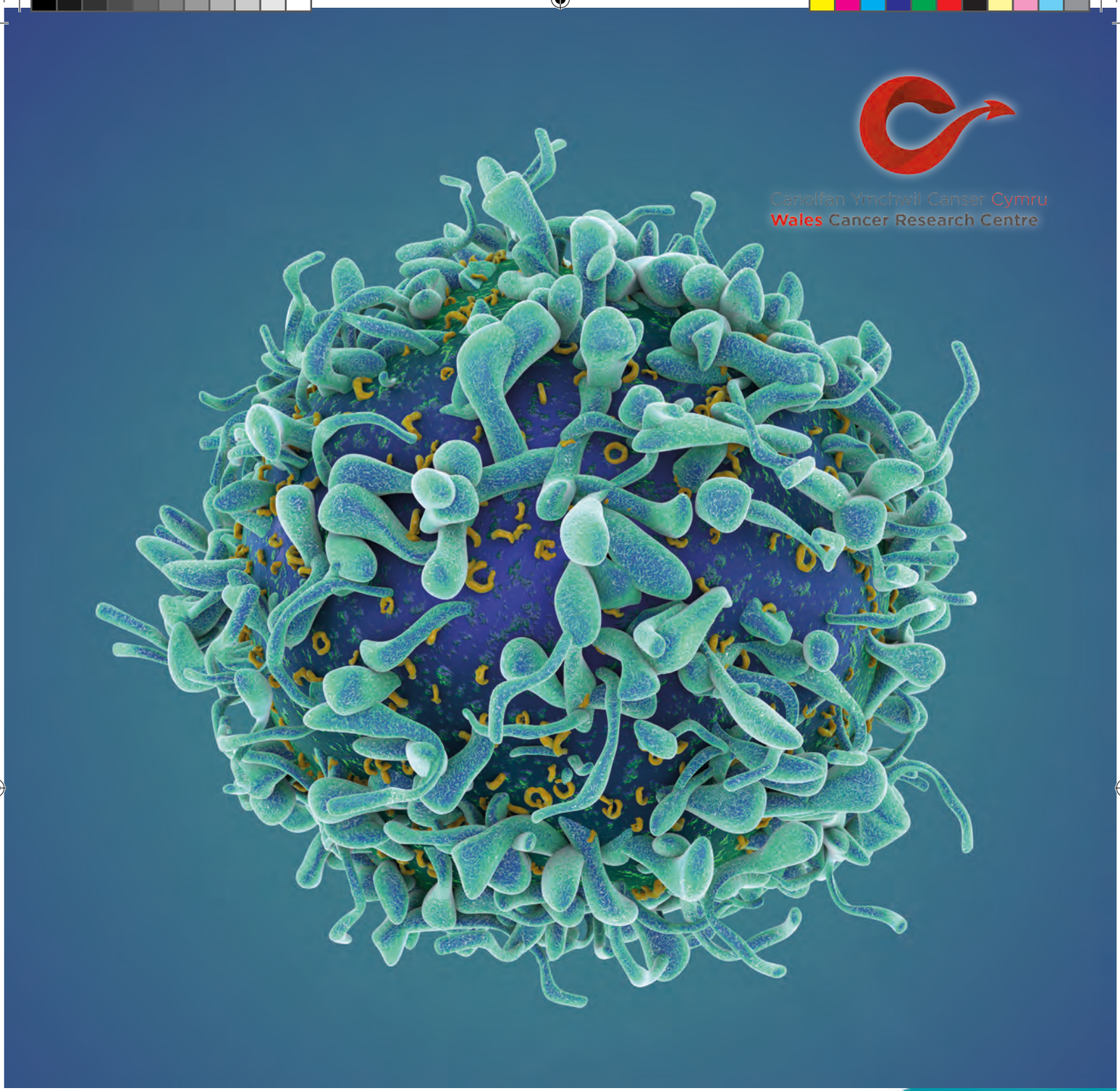


Canolfan Ymchwil Canser Cymru
Wales Cancer Research Centre

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

Ariennir gan **Lywodraeth Cymru**
Funded by **Welsh Government**

2018-19 Annual Report

CONTENTS

The Wales Cancer Research Centre is funded by Welsh Government through Health and Care Research Wales.

This report has been compiled with input from our public and patient involvement group.

INTRODUCTION

"Our vision is to work with cancer patients and other partners to develop and deliver research excellence that benefits the health and welfare of people in Wales and beyond."

The Wales Cancer Research Centre is funded by the Welsh Government and is a key part of Health and Care Research Wales' infrastructure.

We perform and support cancer research of the highest quality, which builds on Wales' international research reputation, with a clear focus on collaboration, innovation and improved patient outcomes.

Our vision is to work with cancer patients and other partners to develop and deliver research excellence that benefits the health and welfare of people in Wales and beyond.

We fund 50 full and part-time posts and aim to improve collaboration in cancer research by bringing these staff and their colleagues together across Wales. Our researchers fulfill a broad range of roles including research nurses, academics, clinicians, pharmacists, pathologists and biomedical scientists.

An External Advisory Board guides the centre in its work. It includes 12 UK experts from across the cancer research spectrum and ensures that our research is of the highest quality and internationally relevant.

The centre is funded by Welsh Government, through Health and Care Research Wales across four broad research themes: pre-clinical, translational, clinical and community.

Above: locations of our staff across Wales

OUR PARTNERS

Prifysgol Bangor University

Prifysgol Abertawe Swansea University

Cardiff University / Prifysgol Caerdydd

GIG CYMRU NHS WALES – Bwrdd Iechyd Prifysgol Aneurin Bevan University Health Board

GIG CYMRU NHS WALES – Bwrdd Iechyd Prifysgol Abertawe Bro Morgannwg University Health Board

GIG CYMRU NHS WALES – Bwrdd Iechyd Prifysgol Caerdydd a'r Fro Cardiff and Vale University Health Board

GIG CYMRU NHS WALES – Ymddiriedolaeth GIG Felindre Velindre NHS Trust

FOREWORD

As we approach our fifth year of funding we have seen an exciting time of change, where we have introduced new posts to improve our work in order to deliver more effective treatments and care to patients.

Since the launch of the centre, I have had the privilege of witnessing some astounding achievements. Our researchers have generated nearly £40 million through the grants they have been awarded, bringing income into Wales. In fact, for every £1 of Welsh Government funding we have received, we have generated £6.50.

Our research outputs have made a significant contribution to the global effort to tackle cancer; to date we have published 364 articles in peer-reviewed journals. The scope of our research means that our work touches every element of the patient journey and will change lives, not just in Wales, but internationally.

This year has seen an expansion of our leadership team with the appointment of three Associate Directors. Prof Duncan Baird, Dr Sunil Dolwani and Prof John Staffurth bring with them a wealth of experience that has helped steer our future direction.

This year we have continued to lead practice-changing research by investing in researchers to develop new clinical trials. We have also funded a consultant to act as the Health and Care Research Wales Cancer Specialty Lead. Dr Rob Jones has been appointed to this role to promote, champion and encourage involvement in cancer trials within NHS Wales, and have an overview of all trials across Health Boards.

Linked with this role, we have employed a part time Project Officer, jointly funded by the Wales Cancer Network. The network is responsible for NHS delivery of cancer services, and close working with them enables us to deliver research that is clinically relevant and that patients are better able to access.

We are improving the geographical range of early phase trials, which will deliver a greater number and variety of new therapies for patients. To help move this ambition forwards, we have employed consultant Dr Mark Davies on a part-time basis to deliver a clinical session in Swansea.

We have also employed an additional research associate post working with Steve Conlan (Professor of Molecular and Cell Biology at Swansea University) and researchers in Cardiff University to advance the development of biological therapies. These include harnessing the power of viruses and the body's own immune system to target cancer, with the hope that we can advance these therapies to clinical trials.

Our community research has expanded with two new posts in the last year. These posts will identify research priorities, develop brain tumour supportive care, progress new trial designs, and progress screening and prevention.

An additional part time Research Associate, Dr Luke Piggott, has been improving our links with the pharmaceuticals industry, marketing Welsh researchers' skills and capabilities externally. This has built on a collaborative, outward-looking culture that we hope will generate further research partnerships and bring income into Wales.

These posts have strengthened the centre through bringing more research funding into Wales, improving research collaboration and increasing the availability of clinical trials to patients in Wales. We hope they will continue to do so as we build on the foundations of our success over the past few years.

Prof. John Chester
Director

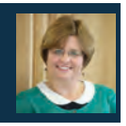
DIRECTOR
Prof John Chester

ASSOCIATE DIRECTOR
Prof Duncan Baird

ASSOCIATE DIRECTOR
Dr Sunil Dolwani

ASSOCIATE DIRECTOR
Prof John Staffurth

OPERATIONS MANAGER
Libby Batt



PRE-CLINICAL

THEME LEAD
Prof Julian Sampson

TRANSLATIONAL

THEME LEADS
Dr Richard Clarkson

Prof Richard Adams

CLINICAL

THEME LEAD
Prof John Staffurth

COMMUNITY

THEME LEAD
Prof Anthony Byrne

PUBLIC & PATIENT INVOLVEMENT

LAY LEAD
Dr Jim Fitzgibbon

ACADEMIC LEAD
Prof Annmarie Nelson

WORK PACKAGE LEADS

Cancer Genetics & Genomic Instability
Prof Duncan Baird

Cancer Immunology
Prof Awen Gallimore

Signalling & Stem Cells
Dr Andy Tee

Stratified Medicine
Dr Richard Clarkson

Prof Richard Adams

Novel Therapeutics & Model Systems
Prof Andrew Westwell

Trials Through to Practice
Dr D Mark Davies

Dr James Powell

Early Phase Trials
Dr Robert Jones

Dr Steve Knapper

Palliative & Supportive Care
Prof Annmarie Nelson

Prof Simon Noble

Screening, Prevention & Early Diagnosis
Prof Kate Brain

Integration & Informatics
Prof David Ford

WALES CANCER RESEARCH CENTRE LEADERSHIP TEAM

LAY SUMMARY

Cancer is a disease no one wants to face, yet one in two of us will develop it in our lifetime. In Wales alone, around 120,000 people are currently living with cancer, and this figure is set to almost double in the next fifteen years.

The Wales Cancer Research Centre is conducting excellent research to improve treatments, clinical decision making and quality of life for patients.

We are building on, and extending, ground-breaking research which has contributed to a doubling in cancer survival in the last forty years. Now half of all cancer patients survive for ten years or more. We are working hard to do even better.

We fund 50 posts at all levels of research, including nurses, doctors, laboratory researchers and pharmacists. Together they carry out research at every stage, from understanding the scientific basis of cancer to developing treatments that improve the health and wellbeing of individual cancer patients.

For instance:

- We are developing new treatments in the laboratory with a focus on genetics, immune systems treatments, stem cell research and drug development.
- We are moving discoveries from the laboratory into the NHS clinical setting with the aim of improving care for current and future patients. We are helping scientists, using samples donated by patients, to understand cancer better for improved patient treatment, diagnosis and quality of life.
- We are giving more patients in Wales the chance to take part in early phase clinical trials using the latest cutting-edge treatments.
- We are helping ensure better support for patients in end of life care.
- We are focusing on screening, prevention and early diagnosis to combat cancer in the community.

Even with all these successes, our work is only partly done. Tackling cancer is a huge, global challenge, but we are successfully treating more cancers than ever before. We believe that, by working together within Wales and internationally, we will meet the challenge.

We hope that the work of the Wales Cancer Research Centre, leading in several areas and collaborating effectively in others, will continue to play its part in improving outcomes for cancer patients internationally.

Public, Patients & Carers

At every stage of our work we aim to involve the public, carers and patients in our research. We believe that they are not just the focus of our research, but should be active participants, working with researchers to plan, manage, carry out and publicise our work. We have appointed, trained and provide on-going support to a team of six members of the public who work with research staff across the Centre. In the last year they have ensured that the research we conduct is relevant, they have contributed to trial recruitment and improved the process for informed consent for tissue donors.

We regularly engage with the public to increase knowledge about the importance of cancer research, and how it's conducted in Wales. We organise events and bring our research to museums, festivals and busy public spaces. This allows the public direct access to our researchers through talks, activities and hands-on tours of our research sites. Our engagement work has impacted on young people's interest in studying science, public knowledge of personalised medicine and improved public awareness of clinical trials.

If you are a member of the public who is interested in getting involved in our research, please email us on WCRC@Cardiff.ac.uk or call 02921 848970.

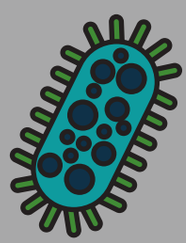
OUR RESEARCH IN NUMBERS

364 articles published in peer reviewed journals

156 grant applications were submitted this year... 65% of these were accepted

£40m £40m income generated through grants awarded in last four years

The equivalent of 82 full time jobs have been created as a result of our activity



8,567 biological samples collected by the Wales Cancer Bank. 23% of these were used in research

7.7

This year's research publications prove their quality by holding an impact factor of 7.7

63 public events held since our launch four years ago

For every £1 invested in the centre, we have generated £6.50

156 public and patient involvement opportunities offered since our launch

NEWSBITES

1 NEW BOWEL CANCER TRIAL

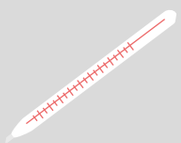
Dr Sunil Dolwani has been awarded an NIHR- HTA grant in order to undertake the CONSCOP2 study – a large randomised control trial looking at whether dye enhanced bowel screening colonoscopy will result in improving long term outcomes for participants. The trial will recruit 3,000 participants in the bowel cancer screening programmes across Wales, England and Scotland.

2 RESEARCH TO YOUR DIGITAL DEVICE

We have brought our research directly to people through digital engagement. In the last year, we have produced 37 web articles, our videos have been watched for over 2,000 minutes and our posts have been viewed 176,000 times on twitter.

3 LEADERSHIP

We continue to develop our people and are pleased to see five members of staff promoted at Cardiff University this year. Three of these were awared the title of professor (more on page 17). Our Future Leaders in Cancer Research programme has been a huge success in developing emerging talent (more on page 27).



4 FUNDING APPLICATIONS

Our coordinating team has helped develop funding applications for the Experimental Cancer Medicine Centre, Cancer Research UK's Radiation Network, the Centre for Trials Research and the Cancer Health Innovation Centre.

5 LUSH STUDY

We are conducting a UK-wide study to understand how people who are high risk interpret and act on possible symptoms of lung cancer and what influences their decision to seek medical help with symptoms. Findings from this study are important to understand how best to support people who are high risk for lung cancer with earlier diagnosis.

6 INCOME TO WALES

Since our launch, we have generated £40 million income through winning grants to continue or expand our research work. This has also generated the equivalent of 82 full time jobs.

7 NEW PATENTS

We have gained two patents though our signalling and stem cell research. Dr Andy Tee is a named inventor with GW Research Limited for the 'Use of cannabidiol in the treatment of Tuberous Sclerosis Complex' and with Indiana University Research and Technology Corporation for 'Therapeutic agent for Tuberous Sclerosis Complex (TSC)'

8 TRIAL RECRUITMENT SUCCESS

We are amongst the top world recruiters for the MONOCLE trial, which treats leukemia.

OUR THEMES

Pre-Clinical research

Our pre-clinical research involves laboratory studies that clarify the mechanisms of cancer development and progression. We identify potential ways of diagnosing and treating cancer that can then be researched and delivered as routine clinical practice to improve patient outcomes.

Work in this theme streamlines and accelerates scientific advances into more effective, safer and more personalised cancer care. The theme covers the following topics:

- Cancer genetics and genomic instability research looks at cancer causing mutations and applies this understanding for patient benefit.
- Cancer immunology research harnesses the power of the immune system to seek out and destroy cancer cells.
- Signalling and stem cell research aims to develop new drugs, validate new therapies and deliver more accurate prognoses for patients.

This stage of research takes the first essential steps towards the development of any new treatment.

Translational research

Translational research involves bringing discoveries from the lab bench to the bedside and back again.

This theme "translates" findings into therapies for patients, and enables scientists, using samples from patients, to understand cancer better.

As different people have different outcomes from cancer treatments, it is important that we identify how best to treat patients in a tailored way.

Our work ensures the benefits of research are translated into clinical trials for patient benefit. We aim to ensure that the right patients receive the right treatment at the right time, and work closely with pre-clinical researchers to identify ways of treating patients with more effective and less toxic treatments.

This work is undertaken in close collaboration with the Wales Cancer Bank and the Centre for Trials Research. Its two main focuses are:

- Novel therapeutics & model systems
- Stratified medicine

Clinical research

Clinical research involves implementing the findings of pre-clinical and translational research. This is the first stage where new treatments are tested in patients. Our clinical theme covers two areas:

- Early phase clinical trials, where new treatments are tested in consensual patients
- Trials through to practice, where the people being studied are randomly allocated one or other of the different treatments under investigation so we can determine the best option for patients

This theme advances knowledge in clinical cancer treatment while providing wider and timely access to newly emerging treatments for patients in Wales. Clinical trial-associated economic activity in Wales is on the rise, partly thanks to our work. We are increasing recruitment to clinical trials across a range of cancer types and ensure that the benefits of trials are moved through into routine practice in the NHS.

Community research

Our palliative and supportive care research differs from others as it focuses on patient and carer, rather than disease related outcomes. Our multidisciplinary team researches across all care settings (including social care), and is establishing a repository of existing research evidence. We engage with clinical teams and policy makers to speed findings straight into practice, and continue to develop high-quality public and patient engagement.

The integration and informatics work we conduct provides digital information systems to underpin the activities of the centre, including data management for clinical trials research and best use of tissue samples donated by patients for research.

Our screening, prevention and early diagnosis research aims to improve understanding of the motivations and behaviours which result in inequalities in uptake of screening programmes, particularly in high-risk, harder-to-reach groups. Through this research we aim to improve screening outcomes and speed up diagnosis, as soon as symptoms occur.

KEY ACHIEVEMENTS

Cancer Research Strategy for Wales

Wales produces some of the world's leading cancer research, and a new initiative has been established to strengthen the nation's outputs. Developing a national strategy for Wales will unite the diverse areas of cancer research conducted here and bring more effective cancer treatments and care to patients as fast as possible. Cancer research strategies have been developed across the UK, and Wales is pleased to now be able to develop its own.

It was advised in the Cancer Delivery Plan for the NHS that NHS Wales should develop a Cancer Research Strategy for Wales (CReSt Cymru). Prof. John Chester (Wales Cancer Research Centre), Prof Tom Crosby (Wales Cancer Network) and Richard Pugh (Wales Cancer Alliance) have come together to lead this strategy with representatives from a variety of research and care backgrounds. This is being programme managed by Rachel Savery, of the Wales Cancer Research Centre and Wales Cancer Network.

The strategy is being developed in collaboration with many organisations working in cancer in Wales and beyond, and is led by Dr Ian Lewis, Head of Strategy and Initiatives for the National Cancer Research Institute (NCRI). It will identify priorities and reflect ambitions of patients, charities, NHS organisations, universities, industry and Welsh Government, and will provide a common goal for cancer researchers in Wales for the next 10 years.

We have launched a year-long process to develop the strategy and establish recommendations to:

- Deliver research with the greatest patient benefit
- Promote the importance of research and development, and enable NHS staff to participate in and conduct research
- Increase commercial and non-commercial clinical trials, bringing more money into Wales and improving patient access to cutting-edge treatments
- Better understand how cancer behaves and how people with the disease are affected

Eleanor Webber works for both the Wales Cancer Research Centre and the Wales Cancer Network. She is part of the team responsible for delivering the strategy. She said, "It's really exciting to be supporting such an important strategy, by bringing the cancer research community together to benefit cancer patients in Wales".

Consultation on the strategy commences in August 2019, and will last for 12 weeks. If you are interested in learning more about the strategy, or would like to share your ideas, please contact us on WCRC@Cardiff.ac.uk.

ASTRA

Facilitating research using tissue samples donated by patients

The Access to Samples for Translational Research (ASTRA) award scheme was introduced in April 2018 to help researchers access patient tumour samples to address new research questions.

We coordinated this scheme and received 23 applications over three funding calls from academic and clinical research groups from Cardiff, Swansea, Bangor including collaborators from Scotland and England. Nine projects were funded in total, providing nearly 800 samples to the research community in Wales primarily through the Wales Cancer Bank.

Projects included the establishment of two new diagnostic tools for lung and colorectal cancers, optimisation of state-of-art blood biopsies for metastatic breast cancer patients, new predictive biomarkers for novel therapeutics in breast cancer, a new collection pipeline for aggressive gastric cancers and their adoption in lab-based research and testing of a new immunotherapy for kidney cancer.

One of the nine projects is now complete, with all expected to reach conclusion by April 2020.

10,000 PATIENTS RECRUITED TO WORLD'S LARGEST PROSTATE TRIAL

The STAMPEDE cancer trial has been responsible for improving the lives of hundreds of prostate cancer patients in Wales.

The trial's 10,000th patient was recruited this year, making it one of the world's biggest cancer trials. This is an incredible achievement for prostate cancer research as a whole, especially here in Wales. In 2005, the very first patient was recruited to the study at Velindre Cancer Centre in Cardiff. Today, STAMPEDE is the largest ever prostate cancer treatment trial, and Velindre remains the largest recruiting centre. Many patients have also been treated on the trial in Singleton, Glangwili General and Bronglais General Hospitals.

Above: The STAMPEDE team at our celebration event at the Welsh Assembly

Above: Tim Driscoll with his wife Mandy and daughter Bethan

Tim Driscoll, 57, from Pontprennau was diagnosed with prostate cancer in 2015. As part of his treatment, he enrolled on the STAMPEDE trial. The electrician and father of triplets said, "Cancer doesn't run in my family and so when the first signs began to appear it never crossed my mind that it could be cancer. I first went to the GP when I developed pain in my joints and my back. Little did I know then, but the cancer had spread to the lymph nodes around my kidney and bladder and was putting pressure on them. After six months of GP visits my cancer was finally diagnosed by a blood test. If they hadn't caught it when they did, I'm told it would've only been four months until it became terminal."

Rugby is Tim's big passion and in his spare time he draws caricatures of Welsh players – as well as other celebrities – and these have been sold to raise thousands for cancer charities. To date, Tim has raised over £30,000. He said, "I'm ever so grateful for the treatment I've received at Velindre Cancer Centre. I've put a lot of time into trying to give something back. Enrolling on the STAMPEDE trial has also helped me feel like I'm giving back. Knowing my experience on the trial will help inform treatments for future patients gives me a real sense of satisfaction. It also means that I have more regular check ups than I would do if I was having standard treatment – it feels like a bit of a safety net, knowing that someone is keeping a close eye on me."

Clinical trials don't guarantee a positive outcome for patients, but fortunately for Tim, STAMPEDE has kept his cancer under control. He has returned to work full-time and is planning to cycle over 100 miles from Cardiff to Oxford to raise money for charity. "I may have cancer," he says, "but cancer hasn't got me!"

Our work on the STAMPEDE trial has led to recruitment figures that make it the largest trial of its kind in the world

The study, which is taking place across the UK and Switzerland, has already demonstrated improved survival with the addition of drugs (both docetaxel and abiraterone) to standard-of-care treatment for men starting long-term hormone therapy.

Professor John Staffurth, Clinical Lead at the Wales Cancer Research Centre, said "STAMPEDE has been a great success story for cancer research within Wales; the high recruitment rate within Velindre owes much to our colleagues in the urology teams across South East Wales, where men are first diagnosed. The research teams within Velindre and Swansea have supported the patients within STAMPEDE for over a decade and we are all delighted that men being diagnosed with this devastating disease now live on average two years longer than they did just ten years ago."

A further four major results will be available in the next five years.

Ensuring that the people at the front line of treating patients have the time and resource to conduct vital research

Building clinical research capacity

The Health and Care Research Wales Clinical Research Time Awards is open every year to staff in NHS Wales or staff contracted to NHS Wales to build research capacity and capability in the NHS by offering staff the opportunity to apply for protected time to engage in research activity. Dr James Powell (Velindre Cancer Centre), Dr Thomas Rackley (Velindre Cancer Centre), and Dr Mark Davies (Abertawe Bro Morgannwg University Health Board) each successfully applied for this award for £87,500 each. This will enable them to develop their Clinical Research activities in brain cancer, head and neck cancer and breast cancer research respectively over the next three years for the benefit of Welsh patients.

Protected time for clinicians to engage in research

We continue to lead practice-changing research by paying for clinicians' time to be protected to engage in research activity. Those offered clinical leadership awards include Professor Dean Harris (Swansea University), Dr Nick Morley (Cardiff University) and Dr James Powell (Velindre Cancer Centre).

Since becoming a WCRC Clinical Leader, Professor Dean Harris has continued to develop the application of a technique called Raman spectroscopy to diagnose colorectal cancer. This technique is non-invasive for the patient, only requiring a blood sample. Professor Harris has received a total of £240,652 of awards for research, including an ASTRA award (Access to patient Samples for Translational Research Award) for £12,500 to set up a pilot study that uses Raman spectroscopy to measure patients' chemotherapy response in colorectal cancer. Professor Harris also received £228,129 from a Research for Patient and Public Benefit (RfPPB) grant to investigate patient acceptability and clinical effectiveness of combined Raman/FIT testing for colorectal cancer diagnosis in primary care. Professor Harris has also applied to Bowel Cancer UK (£149, 605) and AgorIP (£50,000) to develop this research further. Professor Harris has also published his work in four peer-reviewed journals (Analyst, BMJ Open, Gastroenterol Res Pract and Int J Colorectal Dis).

Dr Nick Morley, a consultant radiologist, will be supervising a PhD studentship due to start this autumn. Dr Morley is particularly interested in brain cancers and applied to the Brain Tumour Charity for funding to conduct a study giving an additional scan to patients with glioblastoma (a type of brain cancer) which could have helped identify new clinical biomarkers of the disease, but was unsuccessful. Dr Morley is a member of the recently introduced Brain Multidisciplinary Research Group.

Following his appointment as a WCRC Clinical Leader, Dr James Powell has been awarded a Clinical Research Time Award (mentioned above), which will be due to start this summer. Dr Powell is a co-applicant on a grant awarded by the Engineering and Physical Sciences Research Council (EPSRC) for £780,000 to improve MRI imaging diagnostics for human brain disease. Dr Powell is also a co-investigator on an application for funding of £3.2 million to Cancer Research UK for Cardiff (Cardiff University and Velindre Cancer Centre) to become a member of the new national 'Radiation Network (RadNet)' which aims to develop radiation research across the UK. Dr Powell has also established the Brain Multidisciplinary Research Group (MDRG) in Wales.

TeloNostiX triumphs at Innovation Awards

A test that predicts the aggressiveness of common types of cancer has been crowned 'People's Choice' at Cardiff University's Innovation and Impact (I&I) Awards.

Working in partnership with Cardiff and Vale University Health Board, TeloNostiX – a Cardiff University spin-out – developed a prognostic tool that helps clinicians and patients understand the likely need for treatment and choose the most appropriate course.

Around 350 people voted in the I&I Awards 'People's Choice' social media competition – with more than half casting their vote for TeloNostiX.

The test can forecast the outcome of common cancer types like breast cancer and Chronic Lymphocytic Leukaemia (CLL). It is based on analysing the length of telomeres - caps found at the ends of chromosomes that protect genetic information from damage.

Known as Single Telomere Length Analysis (STELA), the technology has been spun out into TeloNostiX thanks to a 10-year collaboration between Professors Duncan Baird, Christopher Fegan and Christopher Pepper at Cardiff University's School of Medicine.

Professor Baird, who leads our cancer genetics and genomic instability research, said: "We are absolutely delighted to have been voted 'People's Choice' in the awards. We accrued over half of the votes which is testament to the way cancer touches so many lives. Our tests will allow cancer patients and their clinicians to make informed clinical decisions about their disease, and we are looking forward to making the test available to patients in the near future."

Our award-winning work is predicting the aggressiveness of common types of cancer

Industry collaborations

Work towards developing closer links with industry partners has continued over the past year. Establishing these partnerships is key in driving new innovative technologies that can potentially have significant socio-economic impact.

A network including academia and industry partners in translational drug development has been established. This network, consisting of 11 industry and 11 academic partners, covers the broad spectrum of activities required to develop new cancer technologies from concept, within the academic laboratory setting, right through to clinical implementation, at our clinical trials centres. A workshop bringing together the entire network is planned within the next six months to encourage collaboration to accelerate development of novel technologies.

In addition we are currently in discussions to establish partnerships with three commercial businesses. Two of these partnerships will accelerate the development of early stage products by providing business management support and funding that overcomes an existing translational gap where most technologies fail. Using this mechanism, successful products will have the capacity to establish new companies that will be based out of Wales having a direct economic impact. The third partnership aims to bring precision medicine, using genomics, to help guide patient treatment and uncover new areas of interest to research novel therapies for cancer patients.

The development of a new drug that treats cancer that has spread around the body continues, with a new approach and under new guidance we hope to have this drug in early-phase clinical trials in the next two years.

The success of preclinical modelling for new therapies has led to the establishment of a new company in partnership with other platforms from across Wales. The "PDX platform", supported by the WCRC, has collaborated on more than 15 research and commercial projects to further develop new oncology technologies and continues to grow its project portfolio.

UK haematology network

The Cardiff-initiated Experimental Cancer Medicine Centre (ECMC) Haematology Network Group, led by Prof Oliver Ottmann, works with haemato-oncology representatives of other ECMCs across the UK and with the ECMC Network Programme Office.

The primary aim of the group is to develop a UK-wide forum to harness and develop early phase haematology trial opportunities, share work and best practice, and develop national and international links. The first meeting was held at the Hammersmith Hospital (Oct 25th, 2017) and continues to meet on a quarterly basis in locations around the UK. The group has evolved into a cohesive network of members representing haematology departments from the majority of ECMC centres and some non-ECMC sites.

This Network Group, which is in part facilitated by the WCRC, has consolidated its ambitions to develop a UK-wide forum. This forum will look to develop shared early phase haematology trial opportunities, engage in collaborative clinical and translational research, and develop links with partners and industry nationally and internationally. Initially focussing on combination trials, linking joint clinical and preclinical projects, biobanking and immunotherapy, the group has had excellent buy-in from the pharmaceutical industry and Cancer Research UK, being identified as an exemplar in network formation. Membership is continually expanding, emphasising participation by more junior clinical academics and research nurses. In addition, the group is establishing close ties with the existing Paediatric ECMC and the ECMC Immunotherapy Groups.

New drug combination could provide a greater benefit to prostate cancer patients

Results from a trial looking into the effectiveness of combining two drugs (Olaparib and Abiraterone) for patients with a prostate cancer have recently been published in the Lancet Oncology.

Prostate cancer is the fifth leading cause of cancer-associated deaths in men worldwide. Prostate cancer needs the male sex hormone testosterone to grow. Standard treatments for this cancer commonly include hormone therapy or surgical castration to reduce the level of testosterone in your body, but after some time, treatment can stop working and prostate cancer might start to grow again. This is called castration resistant prostate cancer.

Castration resistant prostate cancer is usually treated with hormone therapy, such as enzalutamide and Abiraterone, or chemotherapy, such as docetaxel or cabazitaxel. Sadly, treatment response is often short-lived because the cancer grows resistant to standard treatment. Our researchers are looking for new ways to help men in this situation.

This study was initially a Phase 1b study to test if the drug combination of Olaparib and Abiraterone could be delivered safely. Once this was established it progressed into a phase two trial, an early stage of testing the effectiveness of new treatments in patients.

142 patients took part in the study and were randomly assigned to receive either Olaparib and Abiraterone, or a placebo and Abiraterone. Although those who received Olaparib faced more side effects than those on the placebo trial, this group of patients derived a significant clinical benefit compared to patients receiving placebo.

Dr Rob Jones leads our early phase trials research and was the only UK oncologist named on the paper. Dr Jones said, "Velindre Cancer Centre was the UK's top recruiter to the Olaparib study. We treated 21 patients here in Wales. One of our patients has been on the drug combination for almost five years.

This patient would likely have progressed within three to four months on standard treatment."

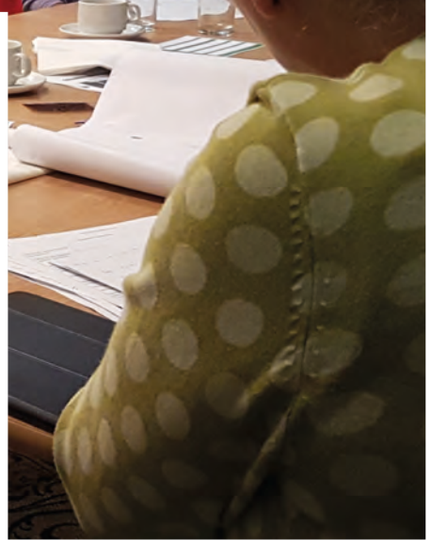
The trial results suggest that the combination of Olaparib and Abiraterone might provide a greater benefit to patients with castration-resistant prostate cancer that has spread to other parts of the body. The trial will now progress to phase three, where a larger group of patients will be recruited to trial the drug and we can more accurately assess its benefits.

Cancer Nurse and Allied Health Professionals Research Network

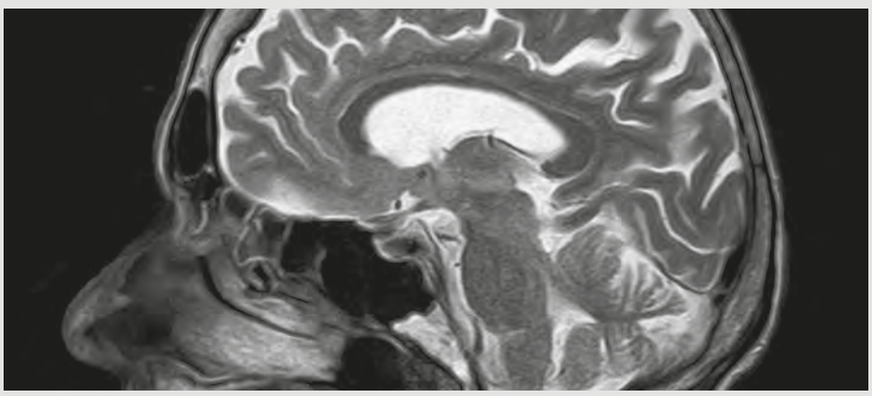
September saw the launch of the All Wales Cancer Nurses and Allied Health Professionals (AHPs) Research Network. We brought together over thirty cancer nurses and AHPs in Neath for a day of talks and group discussion about how the network could provide support o enable staff to undertake research of the highest quality.

The day was led by Profs. Debbie Fenlon and Jane Hopkinson with talks given by a number of nurses and AHPs who are currently conducting their own research.

The network will continue to meet regularly and build on the skills of its members to develop research projects led by nurses and allied health professionals working with patients at the front line. In addition to offering support and training, the network will also facilitate improved communication across Wales.



Brain Multidisciplinary Research Group



Brain tumours have a poor five-year survival rate and are classed as one of the 'cancers of unmet need', highlighting that research into brain cancer needs to be prioritised. With this in mind, we aim to increase the breadth of brain tumour research conducted in Wales and to improve treatments for patients by continuing to support the growing expertise in brain cancer research in Wales. We have helped to launch a Wales-wide multidisciplinary research group (MDRG) focussed on brain tumour research, chaired by Dr James Powell (Velindre Cancer Centre) and Dr Florian Siebzehnrubl (European Cancer Stem Cell Research Institute, Cardiff University). This provides a creative space for clinical and pre-clinical researchers to meet each other and learn about each other's work, in order to develop new collaborations in research. This MDRG has been accepted enthusiastically by the research community across Wales, bringing together researchers from several institutions and disciplines, including surgeons, oncologists, pathologists, geneticists, imaging specialists, speech therapists and scientists. It is anticipated that a brain cancer research strategy in Wales and proposals for research will be developed through the brain MDRG.

The brain MDRG is just one example of a successful group that we have facilitated. Other MDRGs gather around the topics of prostate, lung, breast and colorectal.

The Wales Research and Diagnostic Positron Emission Tomography Imaging (PET) Centre

The Wales Research and Diagnostic Positron Emission Tomography Imaging Centre (PETIC) provides researchers and doctors with a far greater ability to detect malignant tissue and track the effects of drugs in incredible detail. They operate one of the most advanced PET imaging facilities in the UK.

Positron Emission Tomography (PET) scans are unique because they provide functional information which can be very sensitive for detecting small sites of disease anywhere in the body. The facilities are used to diagnose and characterise a range of diseases, particularly cancer, and in some cases to then monitor the effects of treatment and recovery. Both of these aspects are being used to help streamline and enhance the testing of new medicines.

We have recently recruited Dr Nick Morley who is a Consultant Radiologist at PETIC. In addition to supporting the clinical service there, Nick has helped us develop a team to assess the use of PET scans for patients with brain tumours and applied to UK charities who might be able to support that work.

Despite being relatively rare, primary brain tumours and their terrible outcomes have a disproportionate effect on society, causing more 'years of life lost' than cancer from any other site. Dr Morley said, "Many patients deteriorate and die in a number of months, at a relatively young age. Brain cancer can affect thinking, personality and driving, with big collateral impacts on carers and family. We believe that using a PET tracer could help assess the extent of disease and its response to treatment, leading to more tailored treatment strategies and chemo-radiotherapy trial designs that can adapt to patient needs.

"I grew up in Scotland and trained in Edinburgh and Oxford, and it has been really exciting to work in PETIC for the last couple of years. We have enjoyed settling in Monmouthshire and trio siarad Cymraeg! The medical infrastructure in Wales has great possibilities and the support of the Wales Cancer Research Centre has already enabled me to grow a new branch in the network of Brain Tumour researchers."

Promotions

New Professors

Prof. Kate Brain

Prof. Kate Brain leads our Screening, Prevention and Early Diagnosis research. Her work in behavioural science is helping us understand how to reduce the incidence of cancer and how to diagnose it earlier.

She said, "I'm delighted to be awarded a Personal Chair. As a health psychologist based in the School of Medicine, it means a great deal to me personally to have this recognition. Behavioural science and its application to population health have gained considerable ground in recent years, and I'm pleased to have been part of this and to have the privilege of working with a wonderful team of researchers. As a strong advocate of Equality, Diversity and Inclusivity, I hope my promotion success will encourage more women to put themselves forward. Behavioural science is so important because it allows us to gain a deep understanding of the role of human behaviour in cancer screening, prevention and early diagnosis."

Prof. Anthony Byrne

Anthony Byrne, who leads our community research, has been awarded an honorary chair at Cardiff University, according him the title Professor.

He said, "I'm delighted by this acknowledgement from Cardiff University. For me it underscores the commitment of the University to high quality research into complex interventions in palliative and supportive care. I'm indebted to my academic colleagues in the Marie Curie Centre for their expertise and huge commitment in realising our ambitions to be at the forefront of those efforts in Wales, and the UK as a whole. As an NHS clinician the award also, for me, reaffirms the essential nature of collaborations between academia, the NHS and third sector in successfully undertaking and disseminating research capable of changing care. I look forward to supporting expansion of both the depth and reach of our palliative research. In particular I believe there is now even greater opportunity to strengthen the integration of academic and NHS research efforts, with closer alignment of strategies and pathways to clinical impact."

Prof. Annmarie Nelson

Annmarie Nelson is the co-lead of our Palliative and Supportive Care research has been awarded a chair at Cardiff University, according her the title Professor.

She said, "A large part of my work is focused on the experiences of patients and families, and the public perspective. I believe that the best way to understand how patients tolerate disease symptoms, trials and treatments is to ask them directly in real time. At the Wales Cancer Research Centre, not only do we aim to develop cutting edge treatments to understand, prevent and cure cancer, we also want to provide the best care possible when cure is not possible. Aside from our clinically oriented work in trials of interventions for symptom control towards end of life, we look at reducing side effects of treatments, and helping with the late effects of treatment that sometimes happen following cure."

New Readers

Dr. Rob Jones

Dr Rob Jones is the co-lead of our early phase trials research. He heads up the early phase unit at Velindre Cancer Centre where he leads on clinical trials offering the latest treatments to cancer patients.

He said, "I was elated with the news that I had been promoted to Reader. For me it was recognition of the extremely hard work that has been involved in building the solid tumour Phase 1 trial portfolio over the last 5-6 years. This is not only my work but also the 15-20 team members that evolved as our activity has increased. I think it is especially rewarding that the University has recognised the complexities involved in patient care that separates Early Phase research from later phases of clinical research. This means treatment decision-making using drugs that have never been given to patients previously requires a high intellectual input and constant interactions with other Principal Investigators involved with the trial to ensure patient safety."

Dr. Alan Parker

Dr Alan Parker works on oncolytic viruses; his research aims to train viruses to detect and destroy cancer.

He said, "I am naturally delighted to have been promoted to Reader. I am especially grateful to the extremely dedicated and talented team of researchers I have the pleasure of working with, both past and present, without whom this recognition would not have been possible. I can honestly say that I have never felt more excited about our research and the potential of the oncolytic virotherapies we have been generating. We have made significant inroads in developing bespoke virotherapies for targeted cancer applications. The next few years look to be both daunting and exciting in equal measures, as we work closely with our exceptional network of collaborators and funding agencies to translate our exciting pre-clinical findings into meaningful, well executed and timely first-in-human clinical trials."

WALES CANCER PARTNERSHIP

World Cancer Day

We continue to work closely with our colleagues in the Wales Cancer Partnership.

This year we came together to engage with the public utilising the power of our combined digital presences. Working with students from the University of South Wales, we delivered a live Q & A with cancer experts for World Cancer Day.

The panel included Dr Alan Parker (Reader, Cardiff University), Kay Wilson (Senior Research Nurse, Velindre Cancer Centre), Wayne John (patient and volunteer) and Dr Neil Rodrigues (Reader, Cardiff University).

The Q and A session was broadcast across platforms belonging to Cancer Research Wales, Macmillan Cancer Support, Tenovus Cancer Care, Cancer Research UK and the Wales Cancer Research Centre. With our combined impact, the broadcast reached over 4,000 people, helping to spread the message about cancer research to as many people as possible through collaborative working.

CURRENT MEMBERS OF THE PARTNERSHIP

Cancer Quest @Techniquest Glyndwr

Public engagement is at the heart of what we do at the Wales Cancer Research Centre. We have been fortunate enough to work with Techniquest Glyndwr two years running to deliver our Cancer Quest event.

This year the event took place over 27 and 28 of October in their science centre in Wrexham. We brought together collaborators from across Wales, spanning multiple organisations, including:

- Cancer Research Wales
- Tenovus Cancer Care
- Cancer Research UK
- North West Cancer Research
- Betsi Cadwaladr Health Board
- Bangor University

Together, we delivered a fun and engaging event aimed at families, sharing local cancer research and cancer support information.

The event was launched with a performance by Tenovus's Sing with Us choir, who were very warmly received. We ran a series of experiments over the two days including looking at visitors' cheek cells under a microscope, extracting DNA from strawberries and combining liquids that represented medicine. Other hands-on activities included a tour of a giant inflatable bowel, making cells from craft materials and a virtual reality lab tour.

The event was a two-fold success. It brought together researchers who would not normally work together and gave them the opportunity to share the importance of their research with over 600 members of the public.

We hope to work with Techniquest Glyndwr on a similar event in the future.

Delivering cancer services closer to home

Being a cancer patient can be daunting enough, and we like to do all we can to make the lives of patients easier. One of our principal aims has been to improve access to clinical trials for patients across Wales, giving them access to the latest cutting edge treatments. To date we have saved 460 days of travel to research centres in England by opening more trials locally.

Currently all early phase clinical trials (when new treatments are tried for the first time in patients) that open in Wales are managed from Velindre Cancer Centre in Cardiff. When a patient wishes to explore an early phase trial as an option, it requires a visit to the centre in Cardiff. We wanted to make this more convenient still by helping to develop a partnership, known as AWaRe (All Wales Early Phase Research Partnership), between Velindre Cancer Centre and the South West Wales Cancer Centre.

A new information clinic in Singleton Hospital in Swansea spares patients from South West Wales the trip to Cardiff. They can now have an initial consultation in their local hospital, in surroundings more familiar to them. They can learn more about prospective early phase trials and decide if this is something they would like to consider before seeing whether they're eligible to participate at Velindre Cancer Centre. This is particularly valuable for the handful of patients for whom a clinical trial is not suitable as it negates the need for an unnecessary, and potentially disappointing, journey.

Sian Whelan is a Cancer Research Senior Nurse at the South West Wales Cancer Centre. She said, "It's been good to work with the nurses at Velindre Cancer Centre to get this clinic off the ground. Our patients in west Wales can be seen in Swansea to talk about the possibility of entering an early phase trial without travelling to Cardiff for that initial consultation. Before we set up this clinic some patients would make the trip to Cardiff to be told that there wasn't a trial available to them. We are updated by Velindre on a weekly basis so we know if there will be a trial available and we can go through a check list with the patient to look at their trial eligibility here in Swansea. This is just the beginning and we hope the service may be extended in time to provide the treatment locally too."

Kay Wilson, Early Phase Team Lead at Velindre Cancer Centre said, "The collaboration between the two cancer centres has brought our teams together in a way that has huge benefits to patients and their families. This joint working is a fantastic opportunity for Welsh patients and our research community in Wales. Together we can achieve great things to impact patients' experience and outcomes."

The first partnership clinic opened in Singleton hospital at the end of September and runs every Friday afternoon. The first patient has already been seen and the team look forward to welcoming many more to discuss patient participation in research.

Researching treatments for rare blood cancer

Chronic myelomonocytic leukaemia (CMML) is a rare type of blood cancer where there are too many monocytes (a type of white blood cell) in the blood.

Around 450 people develop the disease in the UK each year, but there are few treatments. The disease tends to affect the elderly who cannot tolerate aggressive chemotherapy treatments. Allogeneic stem cell transplant is a potentially curative treatment, but this is only possible in a small minority of younger and healthier patients.

Tefinostat is an oral treatment, that selectively targets monocytes and was tested against CMML in a Phase II trial, known as MONOCLE. The trial, which has recently closed, was led by Chief Investigator Dr Steve Knapper, who leads our early phase trials research. It is a great example of research led from Wales as it was managed by the Centre for Trials Research and followed on directly from laboratory work conducted at Cardiff University.

Dr Joanna Zabkiewicz worked with Dr Knapper on initial laboratory work that led to the drug being trialled in patients. She said, "We were very pleased to be able to transition our initial Tefinostat pre-clinical work into the MONOCLE trial, funded by Bloodwise. I find real value in having the potential to benefit patients with the work that we do. I was also involved in the MONOCLE trial management group. Until now, trial management teams have mostly consisted of clinicians and trial managers, so having scientific input into the trial endpoints and sampling in MONOCLE created a more diverse team."

The trial aimed to determine the tolerability and safety of the drug Tefinostat. Unfortunately the trial didn't show enough clinical responses so was closed after 21 patients had been treated. It is always disappointing when new treatments don't work as effectively as we might have hoped, but stringently testing them in a clinical setting like this is a vital part of research.

Despite the negative clinical results, there is still more we can learn from the trial.

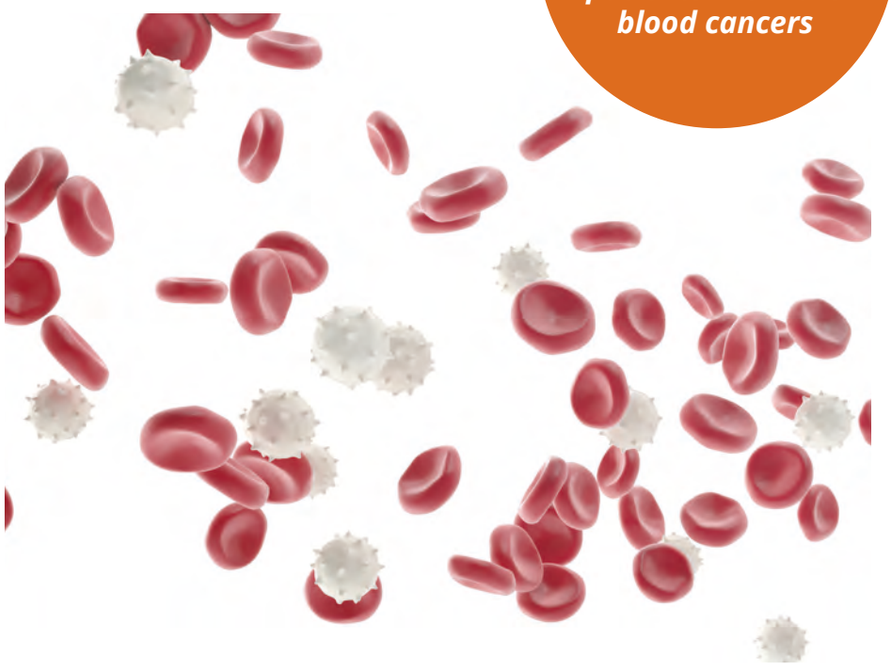
Dr Zabkiewiz added, "The trial allowed us to collect samples from patients for use in further research - something we now plan to do through a clinical fellow post. In collaboration with some of the clinicians involved in the trial, we aim to study some of the mechanisms of drug resistance for this patient group to help us better understand the biology underpinning the disease. This will improve our understanding for future combination therapy design. So, from a science point of view, there are positives. We made some inroads into being involved in the running of the trial, we undertook the trial associated assays and plan to use the data and the samples to further our understanding of this difficult to treat disease."

Dr Knapper said, "MONOCLE may have closed, but we are working on plenty of other innovative trials in Wales. As an example we have recently become the only approved Phase I site in the UK for Novartis blood cancer trials.

"AML is another rare type of leukaemia with few treatment options. We're currently working on a Novartis trial that aims to block proteins that stop the immune system from attacking cancer cells. We've recently recruited 11 patients to this study (CPDR001X2105) which makes us amongst the top world recruiters. We're also proud to be delivering this trial as it is the first trial of its kind that has been made available to AML patients in Wales."

The outcomes of the MONOCLE trial were presented as an abstract at the American Society of Hematology (ASH) meeting in San Diego in December and a paper will follow in 2019.

We are investigating new treatment options for patients with rare blood cancers



First in Wales cellular therapy clinical research collaboration nominated for Nursing Times Award

In 2017, a first of its kind collaboration between research staff from two Welsh hospitals came about to plan the joint delivery of a complex clinical trial for cancer patients. Their efforts have paid off for Welsh patients, and have resulted in being shortlisted for a prestigious Nursing Times award.

The challenges of working across two NHS organisations were overcome by the drive and dedication of both teams to provide safe, seamless care so that patients in Wales could access a new immunotherapy treatment. The outcome of the trial is not yet known, but feedback from the patients indicates that the collaboration itself was a huge success, providing a blueprint for future trials that previously couldn't have been run in Wales.

The Clinical Research facility at the University Hospital of Wales (UHW), and the Clinical Trials Unit at Velindre Cancer Centre had been working together to promote collaboration and cross-site working for 18 months. In this time, staff had spent time in both departments receiving training and support. The clinical trials being delivered by both teams were becoming more complex, and the research teams were able to support each other to manage this while acting separately as two individual sites. In 2016, a new cellular therapy trial for patients with cancer was presented to the research team at Velindre. This involved specialist procedures that could only be carried out in the Haematology department at UHW, but the patients were under the care of Velindre Cancer Centre. The research unit in Velindre was ideal for patients to be seen before treatment started and as follow up. The treatment itself was potentially very risky and needed to be given in a purpose built research facility by trained staff; this was also only available at UHW. Staff from both organisations met with the support of the Wales Cancer Research Centre to discuss how they could work together to deliver the trial.

The nursing teams worked together to decide which visits would be carried out at each site. They also planned a full orientation for patients to ensure they knew who was responsible for their care. The nurses also looked at how to make documentation accessible. Approval was given by the trial sponsor to create a combined study document that could be duplicated and filed at both sites.

The first patient was recruited to the trial towards the end of 2017. The specialist team at UHW were able to retrieve enough cells for the patient to have a full course of six infusions. These were delivered by the research team in the Clinical Research Facility at UHW, and visits between treatments and follow up were taken over by the research team at Velindre Cancer Centre. The results of the trial itself are not yet known, as it is still ongoing. The feedback from the patient and their family was very uplifting. They described the care as seamless, as though both sites were one team. They thanked everyone involved for working together to make it possible, as without this trial there wouldn't have been any other options available to them.

The most important outcome was that patients were able to access a new treatment as a result of this collaborative project. The feedback received reiterated to all involved that patients are at the centre of what we do.

New hope for treating drug resistant breast cancer

Around 70% of breast cancer patients are diagnosed with oestrogen-receptor positive disease, where their breast tumours are sensitive to the fluctuating levels of oestrogen in the body. Oestrogen receptor positive breast tumour cells become 'addicted' to the oestrogen, replicating uncontrollably. This increases the tumour size, and potentially promotes the spread of tumour cells to other parts of the body.

Treatment of this kind of breast cancer can be very effective. Anti-hormone receptor drugs such as tamoxifen and fulvestrant block the effects of oestrogen on these tumours, and have significantly improved the survival rates of breast cancer patients. However, around half of patients receiving these therapies will, ultimately, become resistant to these drugs and may relapse with secondary breast cancers, which may be more aggressive and unresponsive to further anti-hormone therapy.

While it may take many years for these tumours to acquire this resistance, once acquired the treatment options for relapsed patients are relatively limited and often involve aggressive chemotherapy. It is recognised therefore that there is a clear need for new targeted therapies for this at-risk patient group.

Targeted therapies are 'designer treatments' that are aimed at very specific abnormalities within cancers – that may only be present in a small subset of cancer patients, but are highly effective at treating their disease.

A recent laboratory study from a research group at Cardiff University, reported in the international cancer journal Clinical Cancer Research has identified an "Achilles heel" in breast tumours that had previously acquired resistance to the drug tamoxifen.

Patients attending the Cardiff and Vale Breast Clinic in Llandough donated samples of their cancer to the Wales Cancer Bank, an organisation we work very closely with. The research group led by Dr Richard Clarkson used these samples to show that 85% of patients who had developed resistance to tamoxifen went on to develop a sensitivity to an unrelated experimental drug, TRAIL.

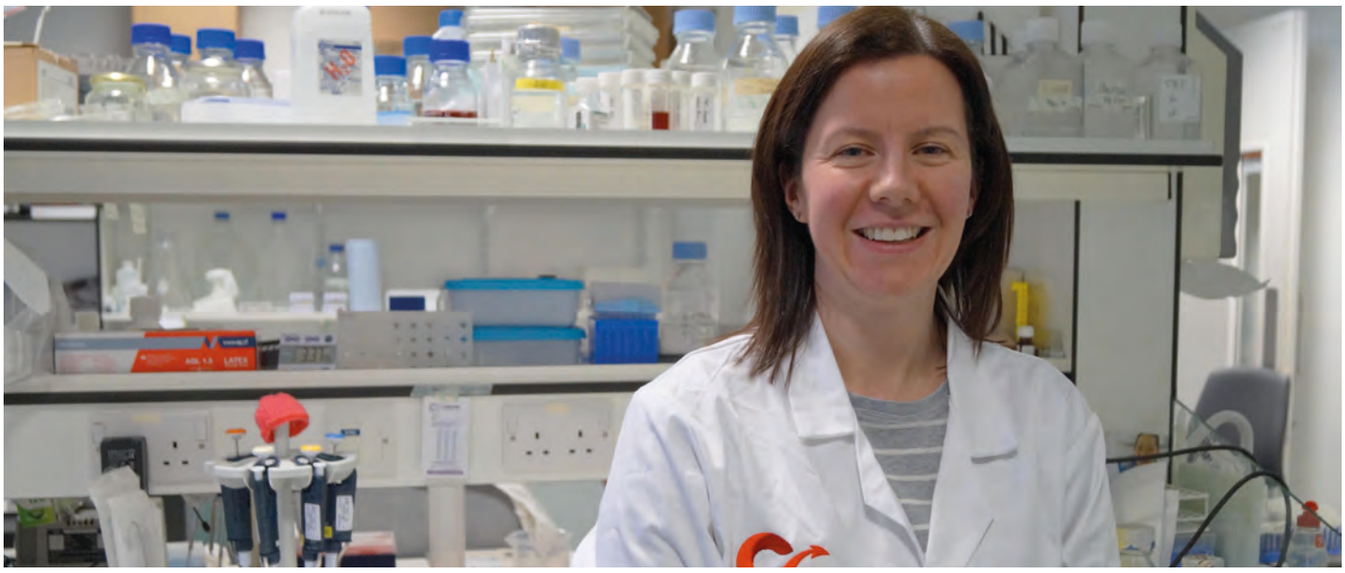
Dr Luke Piggott, the lead investigator on the study, said: "TRAIL is currently not used to treat breast cancer as most breast cancer patients are resistant to it. However, our findings suggest that it could be prescribed for the minority of breast cancer patients who re-present with breast cancer after tamoxifen therapy."

A key finding of this study is that TRAIL is particularly effective at killing the cancer stem cells within these tumours. This means that successful treatment would prevent further relapse and therefore could significantly improve disease-free survival.

"The next step is to test TRAIL in clinical trials," Luke explained. "We hope to lead these trials out of breast clinics across Wales, targeting patients with recurrent disease. We will work closely with the Wales Cancer Bank during these trials to ensure that we maximize the information on the effects of TRAIL in these selected patients."

The Wales Cancer Bank's ongoing mission is to facilitate basic, translational and clinical cancer research such as this, helping to provide improved outcomes for cancer patients across Wales and beyond.

We are pursuing breast cancer treatments that significantly improve disease-free survival.



Wales Cancer Research Centre funding leads to promotion for researcher

We were delighted to hear the recent news that Dr Elaine Dunlop has been awarded a position as a Lecturer at Cardiff University.

Dr Dunlop started working for the Wales Cancer Research Centre in 2015 and we are thrilled that she has attained this sought-after promotion. Half of the new role will involve teaching, allowing her to impart the knowledge she has acquired throughout her career to medical students. On the research side, she has recently secured a grant from the Tuberous Sclerosis Association for a PhD student and being made a permanent member of Cardiff University staff means she can apply for more grants than before.

Our research has shown promise in shrinking TSC tumours in mice. This work will now be tested on sporadic cancers in the laboratory, with the aim of rolling it out into a future clinical trial.

Her research centres on the inherited conditions, Tuberous Sclerosis Complex (TSC) and Birt-Hogg-Dubé (BHD) syndrome where patients are predisposed to develop cysts and tumours. A strength of working on these rare diseases at Cardiff is that the University is internationally recognised for TSC research with established links between geneticists, molecular biologists and clinicians. Dr Dunlop aims to understand what is malfunctioning in TSC and BHD cells at a molecular level, with the goal of identifying weaknesses which could be specifically targeted by therapies. Similarities exist between the altered growth pathways in these genetic diseases and the pathways which are at fault in sporadic cancer, meaning these future treatments could also be effective for the wider cancer community.

In cancer, signals in the cell that control cell growth are overactive. This means the cells will grow out of control and a tumour will form. Dr Dunlop's work looks at a particular growth pathway known as the mTOR pathway. If this pathway could be switched off, it could help prevent the rapid growth of tumours.

She also studies the environment around tuberous sclerosis complex (TSC) cells to better understand the wider influences on cancer cell survival. She collaborates internationally, but has also forged close working relationships more locally too. In Cardiff, she works in collaboration with Dr. Jason Webber in the Tumour Microenvironment Group on vesicles which allow TSC cells to communicate with surrounding normal cells. She is working to see whether this communication pathway supports the growth of TSC cells and if blocking this could prevent tumour growth.

"Being awarded this Lectureship is a huge boost to my scientific career" says Dr Dunlop. "It is a great platform on which to establish my own research team and to continue building on my centre-funded work looking at the mechanisms of cancer growth and how we can prevent it. It also lets me spread my wings academically, through my involvement in the medical education of the future doctors of Wales."

Work like this is vital to understanding how we can tackle cancer in patients. Some of Dr Dunlop's work has shown promise in shrinking TSC tumours in mice. This work will now be tested on sporadic cancers in the laboratory, with the aim that if it shows promise in cancer it can be rolled out into a future clinical trial.

Recovered cancer patient focusses efforts on improving research

On 23rd January the BBC aired a Horizon documentary called "We need to talk about death" focusing on people with incurable conditions and the treatment decisions they need to make. The programme featured local cancer patients, clinicians and researchers.

Julie Hepburn, 64 from Newport, is one of the patients who featured in the programme. She started feeling unwell on Christmas Day, a week after retiring in 2013. "I thought it was a winter sickness bug giving me diarrhoea, vomiting and stomach pain, but it kept recurring," she said. "I went to the GP immediately on return from a three-week retirement holiday in Cyprus. I didn't think it was anything serious at first but being referred on the Urgent Suspected Cancer pathway to a colorectal surgeon did change my mind."

Julie had tests which showed that bowel cancer was present and underwent emergency surgery two weeks later. The cancer was stage three and had gone through the bowel wall, but fortunately had only infected one lymph node. Six sessions of chemotherapy followed at Velindre Cancer Centre in Cardiff after which she was told there was 'no evidence of disease'.

"I was very pleased to receive this news," she said, "but also aware that 40% of people with this stage of bowel cancer would not survive past the five-year mark, so I wasn't yet 'out of the woods.' Once I felt well enough, I wanted to do something positive with my retirement and decided to become involved as a lay representative in cancer research."

Lay representatives are members of the public – often patients or carers – who work with researchers to improve their work. This includes, for example, working with research funders to prioritise research, offering advice as members of a project steering group, commenting on and developing research materials or undertaking interviews with research participants.

Julie also shared her story on BBC Radio Wales. Her interview resulted in a man calling in to say he had the symptoms she mentioned and was now planning to see his GP.

Julie continued, "I started by becoming a lay reviewer for research proposals through the National Institute of Health Research and then discovered the public involvement community in South Wales which advertises opportunities for lay representatives every week on the Health & Care Research Wales website. Now, three years later, I sit on several Trial Management Groups and Steering Committees in the cancer field in South Wales plus a couple of groups in England including a NICE Guideline Committee for Colorectal Cancer. I get a tremendous amount of satisfaction from the work I do providing the patient viewpoint on committees alongside professionals in the field. I feel that I am doing something very useful as well as using the skills I developed in my working life."

One of Julie's major roles is as a Research Partner for our translational theme. Translational medicine covers the part of the research linking laboratory discoveries to the patient and also feeds the knowledge gained from treating patients back into the laboratory to help develop the science further.

Professor Richard Adams co-leads our translational research. He said, "It is so important for us, as researchers, to work with members of the public. We don't want patients to just be the subjects of research - we want to work with them to improve our work. Ideally we create a synergy that answers important medical questions that mean something to the whole team, with the patient very much at the centre of that team. People like Julie are invaluable in helping us achieve this."

Spotlight on: Palliative & Supportive Care

Our Palliative and Supportive Care work stream is conducting research to improve the lives of those with advanced cancer, and the people who care for them.

The four posts we fund and the leads who steer the work are all based at the Marie Curie Palliative Care Research Centre in Cardiff. Together they are committed to developing and undertaking well designed research that will directly improve the care and experience of patients, and their carers, in the advanced stages of their illness.

Public Attitudes to Death and Dying

Some of our recent work with the End of Life Board has resulted in a hugely successful survey about public attitudes to death and dying in Wales. The survey sought to improve our understanding of public perception on the subject to develop informed service delivery. A staggering 2,400 responses to the survey were collected from across Wales. It is encouraging to see such a strong response from the public on this very important subject, and points to a public desire for greater work in end of life research. Results of this survey will be released later this year.

Social Care

The team is developing research around cancer and social care, working closely with Swansea University to build on this area. Following identification of a gap in Welsh care home resident mortality data, our recent work with the Health Analysis and Life Events Division at the Office for National Statistics has helped us to better understand the mortality profile of those that live in care homes, and underpin new collaborations towards future research on the topic. As a result of our published care home reports, we have been contacted by Hospice New Zealand to explore collaborative opportunities.

Another strand of work is the recently completed review of the Cardiff and Vale University Health Board weekend and bank holiday specialist palliative care service. Soon to be published, the evaluation report identifies aspects of the

service that work well, challenges and improvement opportunities and makes recommendations to support the future development and sustainability of the service.

Palliative Care Evidence Review Service (PaCERS)

PaCERS is a rapid evidence review service to support professionals and other decision-makers working in palliative care. The service is unique in responding to requests for evidence from palliative care healthcare professionals on questions of direct importance to their current practice. A critically

appraised summary of available evidence is produced within eight to ten weeks, facilitating at-pace integration of research findings into service development, and helping to embed palliative care research into daily clinical practice.

The service will further improve our engagement with multi-professional clinicians by developing a central web-based repository for access to best evidence. All reviews produced through PaCERS are available to clinicians and other palliative care decision makers at http://palliativecare.walescancerresearchcentre.com/palliative-care-evidence-review-service/

Screening, Prevention and Early Diagnosis

Dr Grace McCutchan and Prof Kate Brain are co-leading the development of a targeted multi-faceted vague cancer symptom awareness campaign, commissioned by Cwm Taf Morgannwg University Health Board. They have been working with the health board, members of the public and healthcare professionals to develop the campaign materials (posters, leaflets, a video for social media and a training session for local cancer champions). The evidence-based campaign is designed to raise awareness of vague cancer symptoms and overcome known barriers to early presentation in deprived groups to highlight the importance of early cancer diagnosis and legitimise help seeking by empowering people to seek medical help with possible cancer symptoms.

To better understand how to support people who attend lung cancer screening to stop smoking, Prof Kate Brain and her team have also been involved in an ongoing trial. The trial will explore if a personalised booklet can motivate people to stop smoking. The booklet contains images of their heart and lungs to show damaged and healthy areas taken from the patient's lung screening appointment, and the development work was led by Dr Grace McCutchan. While the main trial is being led by Nottingham University, Prof Kate Brain and her team are leading the parts of the trial that will understand which elements of the intervention work and why.

To explore how to support earlier lung cancer diagnosis, the Pharmacy Referral for Lung cancer Symptoms (PLUS) study trained pharmacists in deprived communities in Llanelli to screen high-risk patients for possible symptoms to refer for an x-ray if required. The study will explore what patients and health professionals think of the pathway, and Prof Kate Brain and her team will develop an awareness campaign to encourage people with lung cancer symptoms to visit their pharmacist.

Future Leaders in Cancer Research

Cardiff University Future Leaders in Cancer Research (FLiCR) makes financial awards to support early career researchers in their efforts to progress to an independent research career. Funds for the scheme were raised by supporters of Cardiff University who took part in the Cardiff Half Marathon. Although the funding for this scheme comes internally from the University, we are proud to have facilitated this programme in order to identify and build talent in Wales.

FLiCR is a targeted specialist leadership development and support programme for nurturing talent and potential high achievers at Cardiff University. FLiCR aims to invest in talent and build a community of research excellence in Wales. We are looking to tangibly and pragmatically support early career researchers. It is an inclusive programme available for clinical and non-clinical researchers in cancer studies.

Last year's programme saw 18 researchers undertake a programme of activity built to improve their skills as early career researchers. Sessions included:

- Impact and internationalisation
- Film making
- Presentation skills
- Training from Florida's Moffitt Cancer Center to advance the careers of promising scholars
- A writing masterclass with the journal Nature
- A final event where participants showcased their work in a series of films.

The programme also helped some participants to extend their networks by funding international travel to enable them to set up new collaborations and attend internationally renowned training courses.

The scheme has proven such a success that Cardiff University are considering replicating the programme in other research areas.

Public and Patient Involvement

We are committed to Patient and Public Involvement (PPI) and consider it to be the golden thread woven into centre's wide breadth of research. A strategic approach to PPI was taken from the centre's inception with a scoping report carried out at the initial stages and further cemented with a suite of documents including a policy, terms of reference, partnership agreement and standard operating procedures. We are committed to the National Standards for Public Involvement in Research and we have signed up as a 'Freestyle project' with the Public Involvement Standards Development Partnership to test our alignment with the standards. The work has been led by a Lay Lead, Dr Jim Fitzgibbon, Academic Lead, Prof Annmarie Nelson and a Project Officer, Kate Cleary and have appointed six Research Partners to work across the centre's four themes. The Research Partners are involved in various projects throughout the centre and crucially have been welcomed by the researchers and clinicians, creating a culture where the Research Partners are supported and valued.

This year, the Research Partners continue to play a central role in Wales Cancer Research Centre as well as the wider cancer research community and are involved in key projects already highlighted in this report. The All Wales Cancer Research Strategy (CReSt, described on page 10) has four of our Research Partners involved in the strategy's development as members of the Strategic Oversight Board and the Executive Writing Group, ensuring that the strategy will help to reflect views of members of the public in Wales. The highly successful ASTRA funding stream (described on page 10) also had two Research Partners involved in the process as members of the selection panel.

Sarah Peddle and Julie Hepburn are working together to provide PPI input into the recently started ADVANCE Trial which is looking at a way of using a device to improve the pathways for cancer patients at risk of sepsis whilst receiving chemotherapy. They are currently involved in the intial set-up stages of writing patient documentation and questionnaires, attending relevant meetings and gaining ethics approval.

An aim of the PPI programme this year was to raise awareness of PPI in the research community through training opportunities and presentations. Kate Cleary, Jim Fitzgibbon and Sue Campbell have developed a training session on how best to involve the public in research and have delivered the session to various groups within the University including an early career researchers group. Annmarie Nelson has presented on the role of PPI in research at the PhD induction day and this now forms part of the PhD programme. The training session stresses the significance of PPI and highlights the actions that the students need to take as trainer researchers to achieve this. This ensures that the concept and importance of PPI is introduced to researchers at an early point in their career.

The PPI Team contributed a chapter to a book called 'Problem Solving in Person-Centred and Integrated Cancer Care' which was announced in October as the BMA Oncology Book of the Year. The chapter was called 'Embedding Patient and Public Involvement and Engagement in a Cancer Research Centre' and focussed on how the PPI model was established and developed in the centre. The team have also been working on ways to increase diversity in PPI. Jim Fizgibbon has been meeting with our screening, prevention and early diagnosis researchers to understand the barriers to participation in deprived groups.

PACT Study

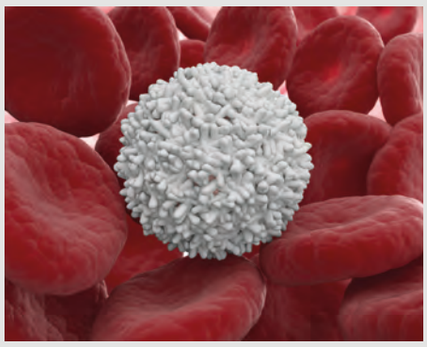
Patient-centred care is essential to the delivery of healthcare; however, this necessitates direct patient involvement in clinical decision-making and can be challenging for patients where there may be misunderstanding of the extent of disease, prognosis and aims of treatment. In this context, decisions are complex and there is a need to balance the risks and benefits, including treatment with palliative intent. The PACT study has examined treatment decision making by multidisciplinary teams of healthcare workers - and between patients and oncologists - in relation to palliative chemotherapy for non-small cell lung cancer. We are collaborating with the Wales Cancer Network to identify immediate opportunities for clinical impact with earlier provision of prompts to incorporate patient priorities and preferences for treatment, and to extend the work beyond lung cancer. It will link this work with the Making Choices Together and Value Based Healthcare programmes as the basis for further integration of research and clinical initiatives prioritising prudent resource use and patient-focused outcomes.

New industrial partnership with Immutep Ltd to develop novel immunotherapeutics

T-cells are a type white blood cell which can find and destroy infected cells. However, to make sure T-cells don't destroy healthy cells, as in the case of autoimmune diseases such as diabetes and rheumatoid arthritis, T-cells have 'molecular brakes' which, when applied, act like off-switches. Cancer cells exploit off-switches, which scientists call 'immune checkpoints' to stop T-cells destroying them. Immune checkpoint inhibitors have been developed which effectively keep T-cells 'switched on' enabling them to kill cancer cells more effectively. Some cancer patients respond extremely well to these novel therapies.

Most patients however, still don't respond. Part of the reason for this may be that T-cells have a number of off-switches and currently only a handful have an approved drug which blocks them. The Gallimore/Godkin laboratory has been working on one of these off-switches namely Lymphocyte activation gene-3 (LAG-3). With support from the WCRC, the group has been looking at various ways of targeting LAG-3 either with antibodies or with small molecules. Small molecules are much simpler than antibodies and are therefore much cheaper to produce. The production of a small molecule, such as aspirin, can be compared to the production of a bicycle which has approximately 150 parts, whereas the production of an antibody can be compared to that of an aeroplane, which has approximately 6 million parts.

Georgina Mason, whose PhD was supported by the Life Sciences Network/Tenovus Cancer Care, has identified small molecules which specifically block the interaction between LAG-3 and its target. She is currently supported by the WCRC to test these molecules in human cell lines to determine which will work best as a LAG-3 inhibitor. This work captured the interest of Dr Frédéric Triebel, a French immunologist who discovered LAG-3 in 1990 leading to an exciting new industrial partnership between Cardiff University (Schools of Medicine and Pharmacy) and Immutep Ltd; a biotechnology company founded by Dr Triebel to develop LAG-3 based therapies. With an investment of around £450,000, the team at Cardiff, led by Andy Godkin, Awen Gallimore and Andrea Brancale, will now push forward with developing LAG-3 targeted drugs which may be tested in clinical studies in the near future.



Speciality Lead

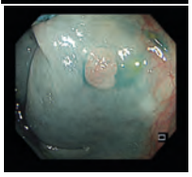
The Specialty Lead for Cancer Role is held by Dr Rob Jones, who leads our early phase trials research. Dr Jones undertakes an active role in developing clinical trials within the NHS and Cardiff University. He is a specialist interested in supporting early phase cancer trials in solid tumours but is keen to see the portfolio of cancer trials expanded in Wales across different specialisms.

The remit of the role is to support the development of trial activity within Wales. He has shared trial recruitment data for each cancer site on a six monthly basis with the clinical community. The trial recruitment data has been collated to enable clinicians and multidisciplinary teams in Wales to have access to cancer site specific information to benchmark and encourage activity. The data has been sourced from the NIHR Open Data Platform (ODP) and provides information on trials and recruitment figures. The ODP includes information on portfolio trials and is one of the most comprehensive and up-to-date databases available. To date this information has been shared across seven cancer site groups and has received positive feedback on both its value and ease of use.

As well as supporting multi-disciplinary teams by providing recruitment information Dr Jones also provides additional, practical, support to make trial opportunities more accessible for clinicians. Information about potential trial opportunities are sent as they arise, and a list of trials open in Wales supports the recruitment data. This enables clinicians to more easily identify suitable opportunities for their patients.

The CONSCOP study

CONSCOP is a landmark research collaboration between Public Health Wales' cancer screening programme and Cancer Research UK.



Our Associate Director, Dr Sunil Dolwani, led the study, which investigated using technology to improve bowel cancer screening. 741 participants were recruited in the bowel cancer screening programme in Wales. These participants attended their screening colonoscopy and were then randomised to receive a blue dye enhanced colonoscopy or a standard white light colonoscopy. We sought to understand whether the blue dye (as pictured), would enable us to detect more polyps - abnormal tissue growths that could become cancerous.

We found that it is feasible to implement this intervention in an NHS bowel cancer screening setting and it was acceptable to both participants and professionals. We found significantly more serrated type polyps and also undertook a health economic evaluation of the costs involved. Based on this, the National Institute of Health Research Health Technology Assessment programme have funded CONSCOP2. We will invite and recruit 3,000 participants, who are undertaking bowel screening, to a further study and follow them up for at least three years to find out if this new approach may find more polyps. If this proves to be the case, we hope it will mean fewer surveillance colonoscopies will be needed and result in improved longer term outcomes from bowel cancer.

Involving the public in CONSCOP

"Being then employed in a police role I recognised the expression on her face. The Nurse was carefully leading my gowned elderly Dad back from an examination of his Bowel. That it was not good news was duly confirmed and within one year he had passed away from amongst us. That event left me with a strong interest in bowel cancer and its treatment.

"Some years later and with more capacity to assist I was very pleased to become a public research partner at the Wales Cancer Research Centre. I could now, as a member of the public, offer commentary on research and, on occasions, draw on that family experience. A trial that I volunteered to become a research partner for was CONSCOP, which was being led by Dr Sunil Dolwani. The detail studied was the use of a vision enhancing dye, sprayed in the colon prior to the colonoscopy (camera examination). Would this enhancement lead to detecting more of the lower lying polyps for removal? An unremoved polyp could be a potential problem for future bowel health. I attended meetings to comment on proposals and progress. How much longer would a patient need to be under examination? Why is the uptake of this trial better in this centre than that one? I could ask away and I was heard.

"Since then I have gone on to be a co-applicant on Dr Dolwani's request for further research funding for CONSCOP2, the extension of the successful first phase study. My own learning has improved and I am convinced of the merit of the enhanced procedure. So I am involved at a level that I can contribute as the public member and I am in my way responding to a need that I first became aware of via my Dad."

- Bob McAllister, patient and public involvement group

EAGLE

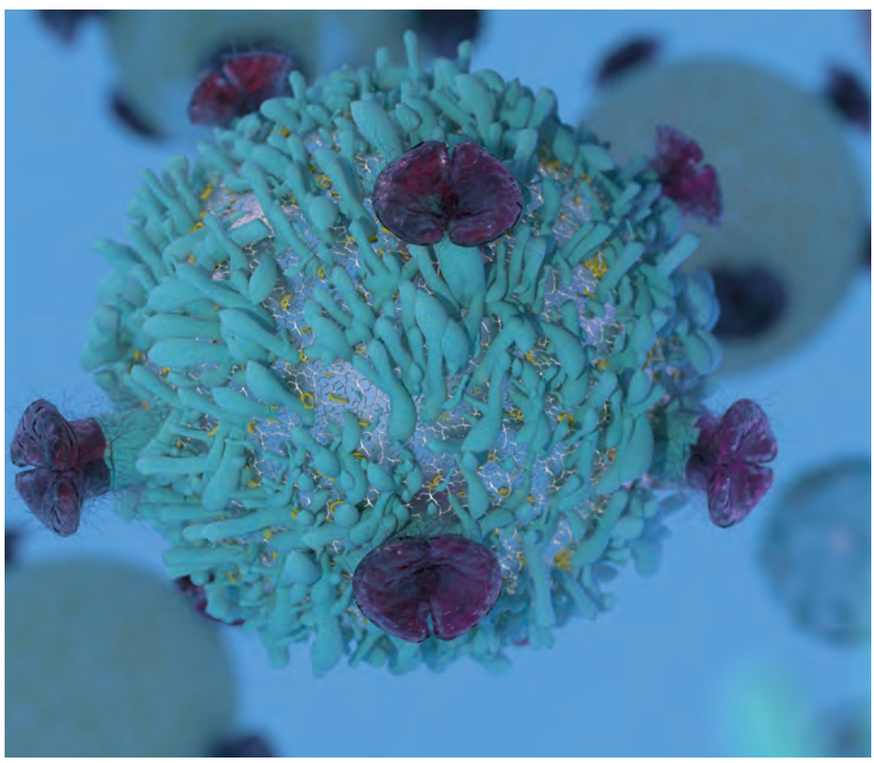
The aim of the EAGLE study was to introduce and evaluate an innovative service to improve the care offered to men and their partners/family in the prostate cancer post-curative treatment setting. The study has already had a direct impact on increasing awareness among healthcare professionals of the need to identify and manage the side effects of radiotherapy. Interviews with healthcare professionals have demonstrated an increase in referrals to gastroenterology of patients suffering from late effects.

Healthcare professionals at the EAGLE sites have reported that their colleagues are now more aware of asking colorectal and gynaecology cancer patients about their bowel function. The screening tool that was successfully validated during this study to highlight bowel issues, ALERT-B, is a concise patient reported screening tool developed to be used at scale, routinely, in clinical and research practice across the UK. This tool has been fully validated and is specified for use in the Royal College of Radiologists 'Modernising radiotherapy services in England'. It is currently being implemented as a patient reported outcome measure on a commercial electronic patient platform. This implementation is focused on NHS England and NHS Wales currently. The work is ongoing as a funded collaboration (clinical fellow) between Macmillan, and the Royal College of Radiologists 2018-2019, and 2019-2020.

Following the success of EAGLE, we are also looking into the late effects of radiotherapy for patients with brain tumours. This is a PhD project that aims to develop a tool that can be used in general clinical settings to assess and refer for specialist care patients that may have treatable cognitive side effects.

Improving the effectiveness of Immunotherapy

Pre-clinical researchers working in cancer immunology recently published the results of a cancer immunotherapy study in the journal Frontiers in Immunology. An emerging area of cancer immunotherapy is the use of a type of cell called a T-cell. T-cells are part of the immune system and play a central role in the immune response. One subtype of T-cells are 'killer T-cells' and these are capable of killing virus-infected cells as well as cancer cells. In cancer patients, the immune system is often suppressed by the cancer, but specially modified killer T cells can be administered to a patient which then bind to a patient's cancer cells and kill them. An example of this is CAR-T cell therapy, which is used to treat some leukaemias – cancers of the blood. Leukaemic cancer cells circulate in the blood so T-cell therapies are injected into the bloodstream and easily find and kill the cancer cells. However, the majority of cancers are solid cancers and can't currently be treated using T-cell therapy, because it is harder for the administered T-cells to find the tumour cells (also known as 'homing') and kill them. This 'homing' process is mediated by the molecule L-selectin, which is found on the surface of killer T-cells. The amount of L-selectin on a T-cell is also an indicator that a T-cell being ready to kill cancer cells. In this study, researchers supported by the WCRC investigated whether increasing L-selectin on anti-cancer T cells would improve homing to the cancer and help to destroy it. It was found that increasing the amount of L-selectin on anti-cancer T-cells improved the ability of T-cells to kill solid cancers. Further investigations found that this was not due to the increased homing of L-selectin enhanced T-cells to the tumour. However, a molecule called CD69, an early marker of T-cell activation was increased only on the L-selectin enhanced T-cells, suggesting that these cells were becoming 'activated' to kill the tumour cells. This is a new discovery regarding the role of L-selectin in T-cell activation. It is hoped that these findings will be used to develop improved therapies for cancer patients.



LOOKING FORWARD

This year has seen our research take on new strides, and we are very excited about the future.

We are shifting the way we look at our work to ensure that patients are, more than ever, at the centre of our research. Instead of research themes, our future work will be divided into two domains:

- The prevention and diagnosis domain will explore personalised prevention and enhanced diagnostics.
- The treatment and care domain will explore improved patient outcomes and optimised patient experience.

With our primary focus on collaboration, we have developed a strong web of partners and links between these organisations and individuals that continues to grow. In the next year we plan to follow up on the success of the 2017 Wales Cancer Conference by working with both the Wales Cancer Network and 1000 Lives to stage another national event for staff and patients. We will also work with MediWales to ensure cancer research is a prominent feature on the agenda at their Connects conference.

Our work on the Cancer Research Strategy for Wales will continue with a consultation period followed by a collaborative effort to bring the strategy's recommendations into effect across Wales.

We will continue to support successful projects such as ASTRA (see page 10) and FLiCR (see page 27), which help with both resources and building future leadership. We are also injecting new life into our translational research committee to help further the work of early career researchers.

Other priorities will include increasing the impact that members of the public have on research and attempting to broaden the membership of our public and patient involvement group.

Our research will also hit the international stage as Dr Rob Jones, who leads our early phase trials research, announces the results of the FAKTION trial at the 2019 ASCO conference in Chicago.

We will be working with Cardiff University to develop stronger links across the institution by developing cross-disciplinary events to bring cancer researchers and clinicians together with their counterparts in departments such as the School of Engineering or the School of Business Studies.

Next year will culminate our initial five year funding period. Each year we have built on the foundations of success built in previous years, and we look forward to what the future will bring as we pursue improved treatment and care for patients in Wales and beyond.

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