News @CRCTU

Summer 2013

www.birmingham.ac.uk/crctu

A busy 12 months for new Director Professor Pamela Kearns

Pamela Kearns replaced Professor Philip Johnson as the Director of the Cancer Research UK (CR UK) Clinical Trials Unit (CRCTU) on the 1st July 2012, just 20 days prior to the submission of the CRCTUs quinquennial review documentation to CR-UK. In October Pam was joined by Neil Steven, Keith Wheatley, Philip Johnson and Lawrence Young to present the CRCTUs 5 year report and future strategy to an independent international review panel convened by CR UK. The panel rated CRCTU as Forefront/Outstanding for both past and future work, a fantastic achievement for Philip, Pam and the unit. CR UK core funding has subsequently been confirmed for another 5-years bring the total number of years the unit has been supported by CR UK to 35.

In August 2012, the Birmingham Clinical Trials Unit (BCTU), CRCTU, and Primary Care Clinical Research and Trials Unit (PC-CRTU) were successful in obtaining funding from the Royal College of Surgeons and CR-UK to host The Birmingham Surgical Trials Consortium. More recently the CRCTU has also been successful in its bid to act as the host clinical trials unit for the Stratified Medicine's Programme National Matrix Study. Two great achievements for Birmingham.

In addition, in the last 12 months more than 15 project grants have been awarded to the unit, 18 trials have opened to recruitment and the CRCTU status as a fully registered UK Clinical Research Collaboration Clinical Trials Unit (UKCRC) has also been re-confirmed. Pam also got to meet JLS!

In recognition of her achievements Pam was promoted to Professor in March 2013.

CRCTU staff congratulate Pam on her promotion to Professor

UNIVERSITY OF BIRMINGHAM

CANCER RESEARCH UK

The new EU Clinical Trials Regulation

Last July, the European Commission proposed a revision of the highly-criticised EU Clinical Trials Directive that will change the legislation from a Directive to a Law that will need to be applied equally in all EU Member States. A principal aim of the revision is to reduce the barriers to academic-sponsored clinical trials. This new legislation, the 'Clinical Trial Regulation' (CTR), is currently under review by the EU Parliament and Member States and is likely to be finalised by the end of the year.

"Overall, I remain optimistic that the proposed CTR will herald the end of disproportionate bureaucracy but we need to continue to raise the profile of what is needed to truly facilitate clinical research in the academic arena. "
Professor Pam Kearns

It is always easy to find fault with EU legislation as it needs to be written to accommodate a broad range of situations in all Member States but the European Commission is to be congratulated in its genuine aim to introduce proportionate regulation. The CTR aims to introduce several new initiatives that if properly implemented will benefit academic clinical trials and reduce (but not totally remove) much of the unnecessary bureaucracy. Four notable changes that will impact on CRCTU trials are

The introduction of the single Portal for application for clinical trial authorization;
The introduction of a full co-sponsorship model;
The requirement for the establishment of national indemnity schemes;
The recognition that not all clinical trials pose an additional risk to subjects compared to treatment in normal clinical practice

Addressing this last point, the CTR proposes a new category of trial in governance terms that will be termed a 'low risk' or 'low intervention' trial. This category will recognise that for some trials participation poses no serious risk to the patient and therefore removes the requirement for additional insurance over and above that already in place to cover clinical practice. This category will be restricted to clinical trials where all the drugs are licensed and used either in their licensed indication or according to standard clinical practice and will allow a reduction in the need for extensive trial-specific drug labelling, accountability and monitoring. Unfortunately, the precise definition of 'low risk trials' remains under debate and the definition may be modified to exclude almost any cancer treatment trial because they have more than a 'very limited and temporary adverse effect'. We are pressing for the definition to be based on the relative increase in risk over standard clinical care and in proportion to the effects of underlying disease.

In addition, the CTR will address the current agenda to increase transparency in reporting results from clinical trials ('AllTrials' campaign). The CTR will mandate a comprehensive end of trial Clinical Study Report, however there is controversy regarding the level of detail within the report. Notably the concept of making publically available full 'line listings' of all data has been challenged by many groups. It is anticipated that in the final version there will be a compromise on the level of detail required in the Report for trials that are not contributing data to the licensed indication of a drug.


Glenis Willmott MEP

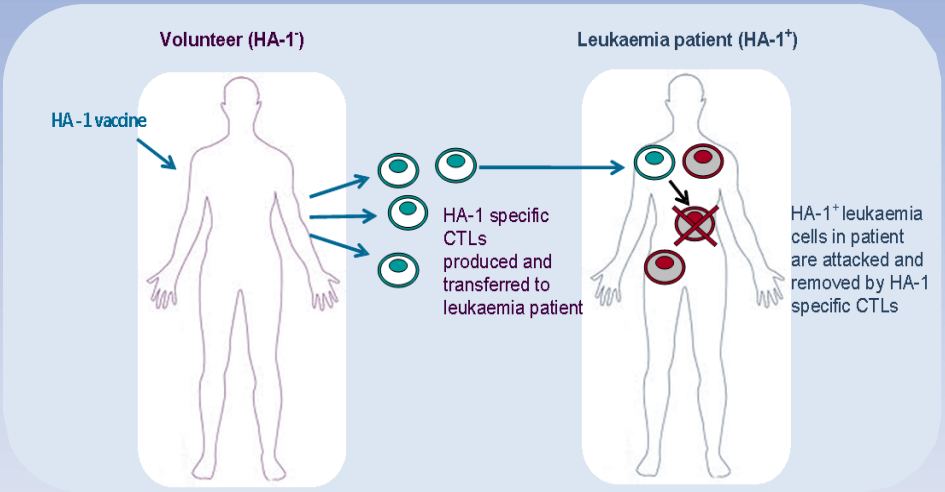
Overall, I remain optimistic that the proposed CTR will herald the end of disproportionate bureaucracy but we need to continue to raise the profile of what is needed to truly facilitate clinical research in the academic arena. To this end, along with the International Society of Paediatric Oncology in Europe (SIOP-E), CR UK and UK CRC, we will continue to work closely with policymakers, most notably with Rapporteur for this legislation in the European Parliament, Glenis Willmott MEP, to ensure the needs of academic cancer research are considered and hope that the final version will be fit for purpose.

HA-1

A World First here in Birmingham

Allogeneic blood stem cell transplants are known to have the potential to cure haematological malignancies and a major component of this is mediated through the donor immune system, termed the graft-versus-leukaemia (GvL) effect. Graft-*versus*-host-disease (G*v*HD) is a common feature of allogeneic haematopoietic stem cell transplants (HSCT) and is a significant cause of morbidity and mortality.

However, patients developing G*v*HD also experience an increased G*v*L effect. A major challenge in improving treatment outcomes is the prevention of G*v*HD while maintaining G*v*L. Both effects are mediated by alloreactive T-cells and it is known that lymphocyte infusions from the stem cell donor (termed *donor lymphocyte infusion*-DLI) can cure patients with relapsed haematological malignancy following an allogeneic HSCT. GvL is thought to be facilitated largely by alloreactive T cells which recognise minor histocompatibility antigens – short peptides which are presented by HLA molecules. HA-1 is a potent and immunodominant minor histocompatibility antigen (mHAg) which is expressed selectively by haematopoietic cells. T-cells against HA-1 are believed to be of importance in the generation of GvL, and the emergence of donor HA-1 specific T-cells in peripheral blood has been shown to be closely associated with disease remission in HA-1$^+$ patients who receive DLI following HSCT.



The HA-1 antigen is an ideal target for therapeutic strategies to enhance the GvL effect in allogeneic stem cell transplant patients. The theory is to vaccinate HA-1$^-$ donors against HA-1 using a DNA and MVA prime/boost vaccination regimen, which has been used to vaccinate against infectious diseases such as HIV and malaria as well as cancers such as melanoma. We have previously shown that vaccination of HLA-A2 transgenic mice with the DNA construct "pDOM", encoding the VLH epitope from HA-1 at the C-terminal end, induces a functional T cell response to HA-1. We propose to use the pDOM-HA-1 DNA vaccine to prime HA-1$^-$ donors and to boost the response with a modified vaccinia Ankara virus (MVA) encoding the same CTL epitope from HA-1 (MVA-HA-1). This first trial will evaluate primarily safety and determine the maximum tolerated dose of the vaccinations in HLA-A2$^+$ and HA-1$^-$ ex-apheresis donors from the Blood Transfusion Service. In addition, the immunogenicity of these vaccines will also be determined.

This trial opened on the 13th December 2012 and one participant has so far completed the vaccination regimen, 1mg pDOM-HA-1 x 2 cycles plus MVA boost (10^8 pfu), with no dose limiting toxicity. We have identified two more participants with the correct HLA type who will complete this first cohort of three, all receiving the same dose. If there are no dose limiting toxicities within the first cohort we will move on to cohort B who will receive 1mg pDOM-HA-1 x 3 cycles plus MVA boost (10^8 pfu).

Centre for Clinical Haematology, Birmingham

BIRMINGHAM CANCER SHOWCASE

How are we fighting cancer in Birmingham?

APRIL 2013

The first Birmingham Cancer Showcase event took place on Wednesday 10th April, visitors attended the Medical School to find out more about how we are fighting cancer in Birmingham. The aim of the event was to showcase the breadth of cancer research taking place at our Birmingham Cancer Research UK Centre.

At the event, visitors were welcomed with a detailed programme explaining all of the event content. Visitors were then shown into the exhibition area in the Wolfson room, which comprised of 15 table top stands and lay posters. Exhibitors included researchers working on viruses and cancer, brain tumours, epigenetics and clinical trials; plus exhibitors from the Pan Birmingham Cancer Research Network, Queen Elizabeth Hospital research team, Cancer Research UK, University of Birmingham and Leukaemia and Lymphoma Research. The Centre for Professional Development rooms included additional displays of CR-UK's online Cell Slider project (http://www.clicktocure.net/), a room all about genes and cancer manned by the teams from the West Midlands Regional Genetics Lab, NHS National Genetics Education and Development Centre and genetics counsellors from Birmingham Women's Hospital, plus drop-in workshops on careers in cancer, patient involvement and health information.

The Leonard Deacon and CPD lecture theatres were used to host 20 minute 'taster talks' throughout the event. Topics included 'An introduction to cancer', 'Using viruses for prostate cancer therapy', 'What is a clinical trial?' and 'How your immune system can control cancer' – picking on areas of specific cancer research expertise in Birmingham. Paul Moss gave the keynote presentation, entitled 'Birmingham's role in bringing forward the day when all cancers are cured.'

"I feel the work being done in Birmingham is very important and has a huge impact on people's lives."

Dragon's Den - Rik Bryan, with Nick James, Pam Kearns, Dan Rea & Keith Wheatley

"Proud to know that my city is playing an important part in this field of research."

The 'behind the scenes' tours of the labs and tissue bank proved incredibly popular. Lab researchers in the IBR West extension surpassed themselves by producing an incredible array of creative displays at their lab benches. Visitors were given a map of the floor, and they could choose which specific displays to visit. These included being shown how skin is grown for HPV research, yeast painting, loading gels, looking down microscopes, cultivating cells... to name a few! Visitors were also given guided tours of our Human Biomaterials Research Centre, to see how patient materials are collected, processed and stored from hospitals across the West Midlands for use in our vital research.

"Without research, there would not be improved testing for various cancers and their treatments. Going through breast cancer myself, I felt I needed to learn more about research, which is proving to be finding a lot of new and wonderful treatments."

The CRCTU staff contributed to the showcase by producing posters to showcase the work within their team and volunteering to help out at the welcome desk and show visitors where to go. The CRCTU stand was a big success with the development of an interactive Snakes and Ladders game to demonstrate the ups and downs of clinical trials, this was only possible with the help of the programming team in particular Bhushan Chhajed and Clive Stubbs Senior Trial Coordinator in Team A. Members of the CRCTU worked shifts to discuss randomisation and clinical trial development with visitors, although some could easily have thought it was have a drink of lemonade and a chocolate egg!

A brilliant 302 visitors attended the event, a mixture of Cancer Research UK supporters, University staff and alumni, local 6th form students, local cancer patients and interested members of the public. A particular highlight was the fantastic "Dragons' Den" finale organised by Karen James and Steve Johnson in Team A along with Hugh Jarrett in the Children's Cancer Trials Team, this was hosted by Rik Bryan, with Nick James, Pam Kearns, Dan Rea and Keith Wheatley acting as the 'Dragons' passing comment and judgement on proposed clinical trials being pitched by the clinicians. Interactive voting keypads meant that the audience also got to have their say, and learn more about the complex decisions involved in cancer clinical trials.

"How fortunate we are to have such dedicated scientists working for Cancer Research UK.

I now feel a renewed energy to fundraise for this wonderful research."

University Hospitals Birmingham NHS Foundation Trust

Birmingham Children's Hospital NHS Foundation Trust

UNIVERSITY OF BIRMINGHAM

CANCER RESEARCH UK

Cancer Research UK Clinical Trials Unit @CRCTU

ASCO | Annual '13 Meeting

Buildin

TO CONG

May 31-June 4, 2013 | McCormick Place | Chicago, Illinois

Presented at Plenary Session

We are very pleased to announce that the aTTom trial was selected to be presented at the Plenary session at ACSO 2013.

The American Society of Clinical Oncology (ASCO) Annual Meeting was held in Chicago on 2nd June 2013 and brought together more than 25,000 oncology professionals from a wide range of specialties**.** The Plenary Session includes several 15-minute presentations highlighting abstracts of scientific research deemed to have the highest merit and greatest impact on oncology research and practice. Only 4 or 5 people a year worldwide are invited to present abstracts at the Plenary Session, so this is a great honour. This year 5306 abstracts were submitted and Professor Richard Gray was invited to present the long awaited results of aTTom.

The aTTom trial (adjuvant Tamoxifen Treatment— offer more?) is a large, uniquely simple, randomised study designed to assess the balance of benefits and risks of prolonging adjuvant tamoxifen treatment in early breast cancer. Tamoxifen is an anti-oestrogen drug that targets oestrogen receptors (ER). It has been shown to improve survival in patients with ER positive (ER+) breast cancer. Previous trials had shown that 5 years treatment was better than 2, but would longer term treatment be beneficial? Between July 1991 and March 2005, 8889 patients were recruited on to the trial from 176 UK centres. All patients randomised to continue tamoxifen completed their additional 5 years of treatment by 2010. Patients remain on follow-up until 2016.

The results of the trial have shown that taking tamoxifen for 10 years rather than the standard of 5 years can significantly lower the risk of dying from breast cancer. There has been widespread press coverage about trial. Dr Daniel Rea, clinical lead researcher based at the CRCTU, said *"These results are important as they establish that giving tamoxifen for longer than the current standard of 5 years significantly cuts the risk of breast cancer returning. Doctors are now likely to recommend continuing tamoxifen for an extra 5 years and this will result in many fewer breast cancer recurrences and breast cancer deaths worldwide. Tamoxifen is cheap and widely available so this could have an immediate impact."*

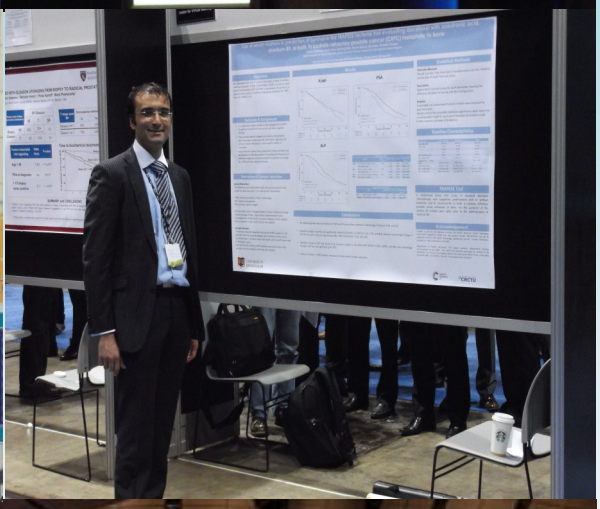
Despite the benefits shown tamoxifen does have side effects. Women can experience side effects similar to menopausal symptoms, such as night sweats and hot flushes. Rare but serious side effects include increased risk of endometrial cancer, blood clots, and stroke. Professor Richard Gray, based at the University of Oxford, previously the Director of Birmingham Clinical Trials Unit (BCTU), said *"Five years of tamoxifen is already an excellent treatment but there have been concerns that giving it for longer might not produce extra benefits and could even be harmful. The aTTom study establishes that the benefits of taking tamoxifen for longer greatly outweigh the risks."*

Tamoxifen is one of the most effective forms of breast cancer treatment currently used world-wide and has saved thousands of lives.

The full abstract text is available at http://meetinglibrary.asco.org/content/112995-132

Prof. Richard Gray (top left), Prof Nick James (top right)

ng Bridges
QUER CANCER



Vivek Wadhwa with poster presentation (centre right)

Trapeze preliminary results well received at ASCO

Trapeze
Taxane
Radioisotope
Zoledronic acid

Trapeze Trial Management Group members Professor Nick James (CI), Sarah Pirrie (Biostatistician) and Ann Pope (Trial Coordinator) recently attended the American Society of Clinical Oncology (ASCO) annual meeting in Chicago to present the preliminary results.

The presentation of the preliminary results was well received and in summary indicated :

- Patients who received Sr89 after 6 cycles of docetaxel experienced improved clinical progression-free survival interval (CPFSI), though not overall survival;
- Zoledronic acid (ZA) did not improve CPFS or overall survival but did significantly improve median time interval prior to first symptomatic skeletal events (SSE) (i.e. SREFI), mostly post progression, suggesting a role as post-chemotherapy maintenance therapy.
- In addition to the increase SREFI , ZA data revealed notably fewer serious SREs, eg. spinal cord compression and associated corrective surgery, as well as substantially fewer SREs as a whole.
- Although Sr89 was statistically significant (based on hazard ratio) it was not necessarily clinically significant.

Further health economic and quality of life analyses are pending.

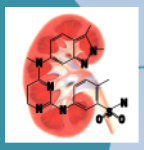
The session Chair, Professor Oliver Sartor, further discussed the results saying that while the reduction in symptomatic skeletal events (SSEs, a term recently coined by the FDA) may be a step forward, we cannot necessarily conclude that zoledronate or denosumab would add benefit when used with agents that independently influence SSEs, e.g. abiraterone, enzalutamide or radium-223.

Subsequent interest from audience members has been high with many requests for slide sets.

Links to the various virtual presentations are available to people who subscribed to or attended the 2013 ASCO annual meeting. The following hyperlinks will take you to Professor James' presentation http://meetinglibrary.asco.org/content/81764 and to Oliver Sartor's discussion http://meetinglibrary.asco.org/content/86723.

The presentation also attracted a feature on BBC Midlands Today as well as coverage in the Birmingham Post.

@CRCTU Trial News



Pazo2

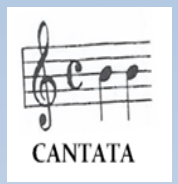
A study of pazopanib efficacy and safety in patients with advanced clear cell renal cell carcinoma and ECOG Performance Status 2

Since the Pazo2 trial opened to recruitment in August 2012, 15 centres have been opened.

With 5 patients recruited to date, recruitment has been much slower than originally predicted. This is related to the potential patient population for Pazo2, who are patients that have been diagnosed with advanced disease and are very poorly. They make up a small number of overall renal cell carcinoma patients in the UK.

The Trial Management Group have taken a pragmatic approach to the eligibility criteria in light of the patient population and a protocol amendment has recently been submitted to change the criteria for clinical imaging requirements. When approved this should make it easier for patients to enter the trial.

A further 15 centres are in setup and will be opening shortly and it is hoped that the impact of the new centres joining will help make the project a success. Interested investigators are encouraged to contact the Pazo2 Trial Office for further information (Pazo2@trials.bham.ac.uk)



A multicentre, phase II randomised controlled trial evaluating docetaxel re-challenge versus cabazitaxel for the treatment of metastatic Castrate Refractory Prostate Cancer (CRPC) previously treated with docetaxel at inception of primary hormone therapy

The CANTATA trial opened at the Queen Elizabeth Hospital Birmingham on 7 March 2013 and has recruited one patient. This trial will assess the safety and levels of activity of cabazitaxel versus docetaxel re-challenge in patients previously exposed to combined docetaxel and androgen deprivation (hormone therapy) as first line treatment for advanced prostate cancer.

Hormone therapy is not curative and all patients will become refractory to standard hormone therapies, with a median time to progression of 18-24 months on first line treatment. Docetaxel in combination with prednisolone was approved by NICE in 2006 for first line treatment of metastatic CRPC (mCRPC), and is currently considered the standard of care for such patients. Based on the results of the TROPIC trial, cabazitaxel, in combination with prednisone or prednisolone, was approved by the US Food and Drug Administration (June 2010) and the European Medicines Agency (March 2011), for the treatment of patients with mCRPC who have previously been treated with docetaxel. Treatment with cabazitaxel is a potential therapeutic option for patients with mCRPC whose disease has progressed during or after docetaxel-based therapy.

Phase I/II feasibility study of cetuximab with 5FU and mitomycin C or cisplatin with concurrent radiotherapy in muscle invasive bladder cancer

The trial is currently recruiting for Cohort 1, Phase I, in which patients receive radical radiotherapy and the drug regimen of cetuximab (a biological therapy) with Mitomycin C (MMC) and Fluorouracil (5FU). The combination of MM C and 5FU increased the effectiveness of radiotherapy treatment in the BC2001 trial. It is hoped that by adding cetuximab, which has shown good radiosensitising results in head & neck cancers, to the two BC2001 drugs that there will be a further increase in radiotherapy effectiveness.

Two sites are currently open and recruiting: Queen Elizabeth Birmingham (opened on 6 July 2012) and Clatterbridge Cancer Centre NHS Foundation Trust (opened on 18 Oct. 2012). Each site has recruited one patient, and these patients are now in follow up. Heartlands Hospital is in set up for Phase I.

DESKTOP III

A randomized multicenter study to compare the efficacy of additional tumour debulking surgery versus chemotherapy alone for recurrent platinum-sensitive ovarian cancer

Standard treatment for first recurrence platinum sensitive ovarian cancer, includes surgery followed by chemotherapy, or chemotherapy alone. DESKTOP I and II demonstrated that surgical patients benefit if they have a positive Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) score: ECOG performance status of 0, no residual tumour after primary surgery (if unknown FIGO stage I/II), and an absence of ascites (less than 500 mL). However, it is not certain if a positive AGO score selects less aggressive tumours, which could be treated by chemotherapy alone, or if it selects patients who will benefit from surgery. The DESKTOP III study aims to answer this question by recruiting 450 patients globally, including 100 UK patients. DESKTOP III opened in the UK in August 2012 and has recruited 6 patients. The strict eligibility criteria make recruitment challenging and more sites are being opened to help reach the target.

UKMCC-01

A phase II study of pazopanib in metastatic merkel cell carcinoma

Merkel cell carcinoma (MCC) is a rare neuroendocrine cancer of the skin with poor prognosis, with approximately 400 cases per year in the UK. MCC typically presents as a cutaneous nodule, most commonly on the head and neck and on the extremities. It disseminates locally as in-transit and satellite metastases, to the regional lymph node basin and more widely to distant skin, lung, central nervous system, bone and liver.

In this single arm open label phase II study, UKMCC-01, we will explore the clinical benefit of pazopanib, an oral multi-targeted tyrosine kinase inhibitor licensed for the treatment of advanced renal cell carcinoma, for advanced MCC. The primary objective of this study is to determine if pazopanib is clinically active, as determined by response rate, in advanced MCC and thus warrants further investigation in a phase III trial.

UKMCC-01 has an additional translational sub-study component that aims to investigate the biology of MCC using tumour samples and paired blood samples before and after treatment. This will involve an assessment of immunity, markers of cell signalling pathways targeted by pazopanib and any evidence of infection with the novel polyoma virus, Merkel Cell associated Virus (MCV). This sub-study will provide the framework to establish a UK wide central biorepository of tissue with associated clinical data from patients with MCC, underpinning future research.

VIT-0910

International randomised phase II trial of the combination of Vincristine and Irinotecan with or without Temozolomide (VI o VIT) in children and adults with refractory or relapsed Rhabdomosarcoma

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children and occurs throughout adult life. Outcomes are poor in metastatic and refractory disease and new treatment strategies are needed.

The primary aim is to evaluate the efficacy of the combination of temozolomide with vincristine and irinotecan (VIT) in children and adult patients with refractory or relapsed RMS as assessed by confirmed objective tumour response. Secondary aims are to evaluate safety, tolerability and efficacy. This is an open-label, multicentre, randomised phase II trial. 80 patients aged 6 months to 50 years with relapsed or refractory RMS who have failed standard treatment, have measurable disease and fulfil all other eligibility criteria, will be randomised to receive vincristine, irinotecan , with or without oral temozolomide. Response will be assessed by CT or MRI after every 2 cycles. Patients may receive up to 12 cycles of therapy in the absence of disease progression. This study will show whether the VIT combination is sufficiently active to take forward into phase III trials in RMS.

Accelerated Hypofractionation, Chemotherapy, Intensity Modulation and Evaluation of Dose Escalation in Oropharyngeal Cancer (ArChIMEDEs-Op)

ArChIMEDEs-Op is a single arm; single centre feasibility study coordinated by CRCTU. The study is funded by Queen Elizabeth Hospital Birmingham Charities and was open to recruitment at University Hospitals Birmingham NHS Foundation Trust in November 2012. We have 5 patients recruited into the study and need another 10 patients to achieve the recruitment target of 15 patients. The study is looking at an increased dose of intensity modulated radiotherapy (IMRT) to treat cancer of the oropharynx. The aim of the study is to see if it is safe and feasible to give a five week schedule (instead of 7 weeks course) of IMRT with standard dose of chemotherapy to treat oropharyngeal cancer in patients that have poor prognosis. It is intended that the shorter treatment schedule will not only reduce treatment time but also increase patient convenience, improve patient treatment compliance and most importantly improve recovery from acute toxicity of chemoradiotherapy.

L u D O

A phase IIa trial of ^{177}Lutetium DOTATATE in children with primary refractory or relapsed high risk neuroblastoma

This is a phase II open label clinical trial that intends to see if patients with neuroblastoma will respond to a new type of treatment called peptide receptor radionuclide therapy using an agent called ^{177}Lutetium DOTATATE, or LuDO for short. The study also looks at the safety of this treatment. LuDO has been given to adults with various types of cancer and this study aims to see if it will help children with neuroblastoma.

To start with 14 patients will be recruited onto the trial, if 3 or more respond to treatment a further 10 patients will be recruited to make a total of 24 patients in the trial. LuDo is given as an intravenous radioactive injection once every 8 – 14 weeks. Patients may receive up to 4 cycles of treatment.

This trial is open to recruitment at University College London Hospital and is accepting referrals from around the UK.

@CRCTU Trial News

GD2

A phase I/II dose schedule finding study of ch14.18/CHO continuous infusion combined with subcutaneous aldesleukin (IL-2) in patients with primary refractory or relapsed neuroblastoma

This is an early phase (I/II) dose schedule finding study of ch14.18/CHO monoclonal antibody given as a continuous infusion where up to 7 different dose schedules with varying infusion durations and total daily doses could be tested. The antibody is given in combination with subcutaneous Aldesleukin (IL-2) and oral Isotretinoin (13-cis-RA) for up to 5 cycles. Participants will have a diagnosis of Neuroblastoma that is either primary refractory (disease has not responded sufficiently to first line treatment) or relapsed (disease has come back). Results from other clinical trials have shown that giving ch14.18/CHO over a longer time period reduces pain, yet the drug still works just as well to fight the Neuroblastoma. The main purpose of this trial is to find out how ch14.18/CHO can be given to children and young people without the need for intravenous morphine so that the treatment can be given in an outpatient setting.

MVA 1b

A Cancer Research UK Phase Ib trial to determine the safety, tolerability and immunogenicity of extended schedule vaccination with MVA-EBNA1/LMP2 in patients with Epstein Barr Virus (EBV) positive nasopharyngeal carcinoma (NPC)

Following on from the Phase I study, the Phase Ib trial has recently opened to recruitment in Birmingham, and will be soon be joined by an additional 6 sites across the UK. Approximately 18 patients with histologically confirmed EBV+ NPC will be recruited over the next 2 years. EBV is a common virus that many people carry without noticing any effects. But the virus is sometimes found in cancer cells and is often found in NPC cells. Researchers hope the vaccine gets the body's immune system to recognise and attack EBV and that it might kill cancer cells containing the virus. The trial is sponsored by Cancer Research UK's Drug Development Office, in collaboration with the University of Birmingham.

Further information can be found at http://www.cancerresearchuk.org/cancer-help/trials/a-trial-of-vaccine-for-nasopharyngeal-cancer-that-contains-epstein-barr-virus.

AdUP

A phase 1 clinical trial of a replication defective adenovirus (type 5) vector expressing nitroreductase and GMCSF (AdNRGM) given via brachytherapy, followed by CB1954, in patients with locally relapsed hormone -refractory prostate cancer

The AdUP trial is investigating potential new treatments for prostate cancer patients whose cancer has returned after being treated with radiotherapy and is no longer responsive to hormone therapy.

The treatment is in 2 parts. The first part is an injection directly into the prostate of modified adenovirus called AdNRGM. The virus is unable to replicate in the body and encodes an enzyme called nitroreductase (NR) and an immune agent called GM-CSF. The second part of the treatment is a pro drug called CB1954. A pro drug is a drug that only becomes active when given with another substance. In this trial, it is the NR enzyme produced by the virus in the AdNRGM injection that makes CB1954 active. In most cells, CB1954 will remain inactive. But when CB1954 reaches the prostate, the NR enzyme will change it into an active drug that can kill tumour cells. The aim of this trial is to investigate the safety of combined treatment with the AdNRGM and B1954.

SCART

Phase I/II study of oral MEK inhibitor Selumetinib (AZD6244 Hyd-Sulphate) in Combination with Highly Active Anti-Retroviral Therapy (HAART) in AIDS-associated Kaposi's sarcoma (KS)

The SCART Trial is aiming to find out the best dose of Selumetinib to give, and how well it works for people who have most common HIV-associated cancer, Kaposi's sarcoma. Selumetinib is a type of biological therapy called a MEK inhibitor. MEK is a cellular signalling protein that is involved in tumour proliferation, therefore blocking this drug may help prevent tumour growth. Patient who enter the SCART Trial taking Highly Active Anti-Retroviral Therapy to help control their HIV infection. The other aim of the trial is to determine how well Selumetinib works to treat Kaposi's sarcoma in people also having this HIV therapy.

BaP

Single Arm Phase II trial assessing the safety, compliance with and activity of Bezafibrate and medroxyProgesterone acetate (BaP) therapy against myeloid and lymphoid

The BaP trial is scheduled to open at four sites in total. Two sites are currently open to recruitment with the final two sites expected to open by the end of July. The first site opened on 20th June 2012 and the first patient was recruited onto the study on 15th October 2012. Since then 7 patients have been recruited onto the study. We have recently implemented a substantial amendment to the trial that now has patients starting Bezafibrate at a considerably reduced dose, which is then escalated weekly until the patient's optimum dose is achieved. We anticipate this will help increase the number of patients staying on treatment in the future.

MAJIC

A RandoMised study of best Available therapy versus JAK Inhibition in patients with high risk Polycythaemia Vera or Essential Thrombocythaemia who are resistant or intolerant to HydroxyCarbamide

MAJIC opened in August 2012 and has recruited 85 patients to date from 30 centres around the UK. MAJIC was the first trial to open from the Leukaemia and Lymphoma Research (LLR) Trials Acceleration Programme (TAP). MAJIC compares a JAK 2 inhibitor, Ruxolitinib, with the best available therapy for patients with polycythaemia vera and essential thrombocythaemia who cannot tolerate the standard treatment. Recruitment has been slightly slower than expected and therefore an amendment to reduce the visit schedule for patients on the control arm has been implemented. The trial is also planning to open a further 5 sites to increase recruitment and geographical coverage across the UK.

RAvVA

Phase II Randomised Trial of 5-Azacitidine versus 5-Azacitidine in combination with Vorinostat in patients with Acute Myeloid Leukaemia or High Risk Myelodysplastic Syndrome Ineligible for Intensive Chemotherapy

RAvVA is a Phase II Randomised Trial comparing Azacitidine versus Azacitidine in combination with Vorinostat in patients with Acute Myeloid Leukaemia (AML) and high Risk Myelodysplastic Syndromes (MDS) who are ineligible for intensive chemotherapy. This trial builds on the Unit's expertise in epigenetic therapies in AML & MDS and extends our previous adjunctive scientific studies to a larger group of patients. RAvVA opened to recruitment on 25th September 2013, 11 months after the grant was awarded. Initially the trial was open to patients with relapsed AML only, however due to a slower than anticipated recruitment rate the trial was amended to include patients with newly diagnosed AML and high risk MDS as well. 10 participating sites out of the 13 Trials Acceleration Programme (TAP) sites have been initiated and opened to recruitment. There are a further 4 non-TAP sites in set up. 13 patients have been randomised to date. The target is to randomise 160 patients over a 24 month period.

De-Iron

De-Iron: A phase 2 study of the efficacy and safety of Deferasirox administered at early iron loading in patients with transfusion-dependent Myelodysplastic Syndromes

The De-Iron trial is now open at 5 centres with an additional 15 sites in set up. We are currently open to the inclusion of up to 5 more sites that are able to swiftly facilitate the set-up process. The first patient was recruited onto the trial on 19th June 2013 from Dr Killick at Bournemouth and there are a further two patients in pre-screening. Recruitment has been slower than expected due to the realisation that a patient's serum ferritin can rise above the threshold stated in the inclusion criteria soon after the patient reaches the definition of transfusion dependence. Now that this issue has been identified, open sites are tracking newly identified patients as they become transfusion dependent, which seems to be a much more successful strategy. Formalised guidelines on identifying De-Iron patients is in preparation and should be available soon.

@CRCTU

Public engagement news

On 7th July Karen Doyle (Cancer Research UK Snr Nurse) went along to Cheltenham Racecourse to speak at the opening of Cancer Research UK's Race for Life. It was such a great day, lovely weather and the new event site in front of the grandstand worked really well for participants and spectators – especially because of the shade it provided! Despite the hot weather there were 3775 ladies taking part in the 5k and 10k events and they are hoping to raise £215,000.

On the 20th May was the UHB Research Showcase and the unit had various people helping Debbie Ringham organised a CR UK Centre stand to showcase what clinical trials are, those helping out were Karen Doyle, Clive Stubbs, Bhushan Chhajed, Davina Scott, Libby Marcus, Anna Rowe and Jayne Doran.

Darren Barton helped out on the NIHR Liver stand and the breast team worked with Adele Francis to randomise penguins.

The Clinical Haematology team Tina McSkeane, Ade Faleti, Sarah Essex, Julie Arrazi and Shamyla Siddique – Ramblers for Research - did a impressive 10 mile walk for Cure Leukaemia for Kids on the 19th May 2013 and raised £578.

Cara Williams completed a half marathon in 2 hours, 44 minutes on the 8th of October and raised £271 for Leukaemia and Lymphoma Research. The sore muscles were well worth the money raised! Well done Cara!

UNIVERSITY OF BIRMINGHAM

CR UK Clinical Trials Unit

School of Cancer Sciences
University of Birmingham
Edgbaston
Birmingham B15 2TT

Contact@CRCTU

Ph. 0121 414 8040
Fax. 0121 414 3700
Email. CRCTU-GeneralEnquiries@trials.bham.ac.uk
newbusiness@trials.bham.ac.uk
Web. http://www.birmingham.ac.uk/crctu