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People often tell us they don’t know much about what we do beyond the discovery, manufacture, and commercialisation of our current licensed medicines. We’re using our skills and resources to work with the NHS and other partners in many areas of cancer research and care.

Focused on what truly matters

Date of preparation: August 2012. ONC12-091
Acknowledgements: NCRI partners

The Scientific Committee and organising team are grateful to all the NCRI partners for their continuing commitment to the concept of a multidisciplinary cancer conference and for their financial support.
I am delighted to welcome you to the ninth NCRI Cancer Conference in my first year as Chair of the NCRI.

This next Conference plays a very important role in bringing researchers together from the UK and internationally. Over the four days, you will have the opportunity to take part in sessions and meet with colleagues from across the world and across the spectrum of cancer research: basic science, clinical studies, translational science, palliative care and end of life care.

Each year we attract established experts, along with students and other early career researchers from a range of disciplines, as well as patients and carers with an interest and involvement in research. This diversity is one of our strengths. With the huge range of work on display, everyone has the opportunity to learn something new. A group of 50 A level students from the Liverpool area will also be with us on Tuesday to take part in a schools programme and we hope that some of them will be inspired to follow a career in cancer research.

The NCRI Partnership is comprised of 21 government and charity funders of research together with the Association of British Pharmaceutical Industry (ABPI). We aim to coordinate research and funding strategies, for the ultimate benefit of patients and public. Communication is the key to this, whether it be among scientists and clinicians, among funders, with policy-makers, or the general public. NCRI has many initiatives promoting communication, coordination and collaboration of which this annual Conference is perhaps the most visible. Find out more about NCRI and our other initiatives by visiting our stand in the exhibition hall.

The Conference is a joint effort from many people. I would like to thank the sponsors and exhibitors, including the NCRI partners, who help to make the event happen. I would also like to extend my thanks to the Scientific Committee for developing an inspiring programme, and of course the speakers themselves who have travelled from all over the world to come and speak in Liverpool. Finally I am grateful to the Conference team within the NCRI Secretariat for their excellent organisation. Thank you to everyone for making our Conference such a great success.

Enjoy your Conference experience.

Harpal S Kumar
Chair of the National Cancer Research Institute
Welcome from the Chairs

Message from the Chair of the Scientific Committee
Professor Gerard Evan
Chair of the 2013 Scientific Committee
Head of Department of Biochemistry, University of Cambridge, UK

On behalf of the Scientific Committee, it is a pleasure to welcome you to the vibrant city of Liverpool and the ninth NCRI Cancer Conference. If you want to understand cancer, and to help people with cancer, then you are in the right place.

Colleagues on the Scientific Committee deserve my gratitude for building a programme combining the best international research with opportunities for interaction and networking.

There are several types of talks for you to choose from, such as plenary lectures, parallel sessions, symposia, and proffered paper sessions. Talks and posters cover the whole spectrum of cancer research, from basic research and translational science, through to clinical application in diagnosis and treatment, as well as sessions on survivorship, end of life care and health service research. We aim to challenge the way you think about your own research and its place within a broader context, contributing to an overall understanding of cancer and how best to help cancer patients.

Amongst the busy programme there will be sessions aimed at surgeons, oncologists and scientists on Monday in a ‘Working together in surgery’ track. Plus, after the success of last year’s collaboration with the Royal College of Radiologists (RCR), some sessions on Tuesday have again been programmed in association with the RCR. Tuesday also sees the ever-popular Clinical Trials Showcase which provides updates on practice-changing trials, these events making this the essential day for clinicians to attend.

Please also make time to visit exhibitors in Hall 2. There are more than 60 stands from different companies and organisations. Join us there in the breaks to hear about their latest products and services, and acknowledge their contribution to the Conference.

Finally, if you use technology to help with your networking, sign up to the NCRI group on LinkedIn. There will also be a prize for the best tweet of the Conference for all you tweeters. Use #NCRI2013 and get tweeting.

Wishing you an enjoyable and rewarding stay in Liverpool.

Gerard Evan
Chair of the 2013 Scientific Committee
Head of Department of Biochemistry, University of Cambridge, UK
The NCRI is grateful to the Scientific Committee for their support in developing the programme and maintaining the high standards of this Conference.
Support grants are provided towards the 2013 programme, which has been designed independently by your peers (see Scientific Committee on page 4).

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*Amgen Oncology has provided unrestricted funding to enable this conference to take place. Amgen Oncology has a stand at the Conference but has had no input into the programme, selection of speakers, topics or awards.
Useful information

Accommodation
For accommodation enquiries, please visit the Accommodation desk in the registration area.

Browsing abstracts
All abstracts are available to view online at conference.ncri.org.uk/abstracts/2013/search.html
These web pages have been optimised for viewing with smartphones. The abstracts are also on the USB stick in your delegate bag. USB sticks are sponsored by Nature/BJC.

Car parking
Convenient parking is available opposite the BT Convention Centre at a cost of £10 per 24 hours.

Choosing your sessions
While every attempt has been made to put popular sessions in large rooms, some sessions may be oversubscribed on the day. Entry is on a first come first served basis, so please arrive early at your chosen session.
As a courtesy to speakers and other delegates, please remember to turn off your mobile phone before entering the lecture halls.

Please wear your delegate badge at all times while at the venue and social events.

Cloakroom and lost property
A cloakroom is provided at the entrance of the BT Convention Centre. NCRI does not accept any liability for lost property. Please visit the BT Convention Centre helpdesk in the entrance to report or reclaim lost property.

CPD certificates
The 2013 NCRI Cancer Conference has been approved by the Federation of Royal Colleges of Physicians for 24 category 1 (external) CPD credits. Request your CPD certificate from the General Enquiries desk when you hand in your badge before you leave the Conference. Your certificate will be sent by email.

Exhibition hall
The exhibition runs from Sunday 3 November to Tuesday 5 November in Hall 2 of the BT Convention Centre. Exhibitors contribute significantly to the financial sustainability of the Conference. Please make sure you visit relevant exhibitors and acknowledge their support. A full list and a map are provided from page 172 of this book.

Feedback
Your feedback helps us tremendously when planning future Conferences. Please take a few minutes to complete the online survey, which will be sent to you after the Conference.
If you want to leave feedback immediately, please visit the General Enquiries desk.
General enquiries
Please visit the General Enquiries desk situated in the registration area between Sunday 3 and Wednesday 6 November, where NCRI Cancer Conference staff will be happy to help. Contact us on +44 (0)151 239 6065 or +44 (0)151 239 6066. Out of Conference hours, please call: +44 (0)7539 477 105 or +44 (0)7539 477 109.

Messages
A message board is available in the main registration area. To leave a message with the Conference staff, please call +44 (0)151 239 6065.

Passport competition
Your bag contains a passport competition book. Once your book has been stamped by all of the participating exhibitors, drop it into the competition box situated outside Hall 2 on the exhibitors helpdesk for a chance to win some great prizes.

Poster sessions
Posters must be put up by 08.30 on the day of your poster session and remain on your poster board until 17.40. Posters are available for informal viewing throughout the allocated day of their presentation. Presenters are encouraged to provide handouts for when they are not present to speak to participants.

To avoid overcrowding during the poster presentation times, poster presenters are asked to stand with their posters for only half of the session as noted in the timetable below.

### Poster session A: Monday 4 November
- Odd number posters: 10.20–11.20
- Even number posters: 13.30–14.30

### Poster session B: Tuesday 5 November
- Odd number posters: 10.20–11.20
- Even number posters: 13.30–14.30

Posters must be taken down by 17.40 on the allocated day. Posters left up after this time will be removed. The Conference Secretariat is not responsible for storing posters that have been removed.

Press office
The Conference press office is located in Room 5 on the first floor. To contact the press team, please call +44 (0)151 239 6060, +44 (0)151 239 6061, +44 (0)151 239 6062, +44 (0)151 239 6063 or +44 (0)151 239 6064. Out of Conference hours, please call +44 (0)7050 264 059.

Recycling facilities
The BT Convention Centre is one of the most eco-friendly meeting venues in the UK. Please use the facilities provided to recycle paper. If you wish to recycle your bag, badge and lanyard, pass them to the Conference staff.
Registration

Registration is situated in the foyer on the first floor and is open at the following times:

- Sunday 3 November 13.00–19.30
- Monday 4 November 07.45–19.30
- Tuesday 5 November 07.45–19.30
- Wednesday 6 November 08.15–13.00

Screening of ‘the Enemy Within: 50 years of fighting cancer’

Vivienne Parry OBE tells the incredible story of our fight against cancer over the last 50 years. Through the eyes of scientists, researchers and patients, we see how far we have come and how far we have to go. Including contributions from Professor Robert Weinberg, Professor Umberto Veronesi, Lord Ara Darzi, Cancer Research UK, David Nathan, Brian Druker and many more.

The film is a non-commercial, editorially independent piece of work which has been supported by Cancer Research UK and funded by an educational grant from Roche.

The film runs for approximately 70 minutes. It will be screened as follows:

- Sunday 3 November, Room 4: 13.30
- Monday 4 November, Room 7: 07.45 and 18.00
- Tuesday 5 November, Room 7: 07.45 and 13.00
- Wednesday 6 November, Room 7: 08.00

Taxis

A taxi rank is situated on the riverside entrance of the BT Convention Centre. Alternatively, please call +44 (0)151 298 2222 or +44 (0)151 207 2222.

Twitter competition

Let’s get NCRI trending. Use #NCRI2013 to tweet your experiences, thoughts and highlights of the Conference. Follow us @NCRI. The best tweet of the Conference will win a £100 Wisepress book voucher.
Choosing the right session

Plenary lectures
These feature experts from the UK and overseas, invited by the Scientific Committee to give plenary lectures. All have been briefed to give talks that are accessible to a broad audience. Their talks may address a broad area of work, summarise their own research, or discuss an important area of policy relating to cancer. There are plenary lectures on each of the four days of the Conference.

Symposia
Each symposium comprises three talks from speakers of international standing around a broad theme. The aim is to consider one topic from three different angles, with a mix of disciplinary approaches. A symposium may cover basic, translational and clinical research, or it may reach into areas such as social and behavioural studies, as well as approaches to prevention. Symposia should help you to see your own work within a broader context of studies beyond your own expertise.

Parallel sessions
These more specialised sessions mainly attract professionals in the areas on which they focus. On each day there will be one parallel session organised by consumers and intended to be accessible to a lay audience, though professionals frequently attend these sessions too. Parallel sessions cover a range of themes; see page 11 for further information.

Workshops
Workshops are organised on a demand-led basis and vary somewhat in format. Some are educational or commercially-led training sessions, while others debate a hot topic or discuss the availability of research resources such as biosamples or datasets. Workshops are intended to include more audience participation and are essentially discussion forums.

Proffered paper sessions
From among the abstracts submitted each year the Scientific Committee pick out a number of high quality abstracts for oral presentation in proffered paper sessions.

Clinical Trials Showcase
The Scientific Committee select abstracts on clinical trials from those that are submitted. Trials selected for presentation in the Clinical Trials Showcase are often practice-changing, of high quality or are presenting new data.
Session themes

Diagnosis and therapy
Screening technologies and diagnostic markers.
Estimation of prognosis and identification of individuals at increased risk of cancer.
Factors associated with stage of diagnosis and clinical outcome.
All types of therapy and all phases of development and testing.

Epidemiology and prevention
Population-based research aimed at understanding causation, incidence, trends, and risk (such as environmental and genetic risk).
Research on prevention, e.g. lifestyle and nutritional factors, including individual and community interventions.

Health services research
Quality and cost of healthcare and coordination of care.
Development and testing of healthcare delivery methods.
Access to healthcare including primary care and screening services.

Information, patients and the public
Public policy issues, ethics and confidentiality.
Education and communication about cancer.
Involvement of patients and public in deciding research priorities.
Patient-led research.

Survivorship and end-of-life care
Living with and beyond cancer: Physical, psychological and social impacts and their management.
Research into care at the end of life.

The cancer cell and model systems
Molecular and cellular mechanisms of oncogenesis and tumour suppression.
The tumour microenvironment.
Cell biology relevant to cancer.

Tumour-specific research
Tumour-specific research, including basic, translational, and clinical approaches.
Research applied to specific patient groups, such as paediatric patients, and older people with co-morbidities.
The Royal College of Radiologists’ Faculty of Clinical Oncology and the 2013 NCRI Cancer Conference

The Royal College of Radiologists (RCR) is delighted to be working with the NCRI again to bring you some exciting sessions delivered by a world-class faculty to the 2013 NCRI Cancer Conference on Tuesday 5 November.

Join your RCR colleagues for these talks. See the full programme for Tuesday from page 84.

10.20 – 11.20
Poster viewing, including a dedicated radiotherapy and radiobiology section

11.20 – 12.50
Latest developments in radiotherapy for breast cancer
Hosted by Alastair M Thompson, Dundee Cancer Centre, UK

13.30 – 14.30
Poster viewing, including a dedicated radiotherapy and radiobiology section

14.30 – 16.00
Proffered paper session

After lunch, the College will host a proffered paper session. One of the presentations in this session will be awarded an RCR Ross Prize for the best oral presentation, as judged by an RCR judging panel.

16.20 – 17.50
Clinical application of translational research in breast cancer
Hosted by John Yarnold, The Institute of Cancer Research, London, UK
Networking

Take advantage of the opportunities at this year’s Conference to network with old colleagues, meet fellow participants and speakers and start new collaborations. We have a number of exciting and inspiring events for you to take part in, including:

**Opening reception**
Sunday 3 November, 18.00 – 20.00, Hall 2

Join fellow participants for a light dinner and drinks in the exhibit hall. Use this opportunity to visit exhibitors and hear about the latest initiatives, services and products from over 70 organisations.

**Early career scientists dinner**
Sunday 3 November evening

Are you a student or postdoc? Colleagues from Liverpool have generously volunteered to guide you through town and make sure you connect with each other, while discovering the local scene. Tables have been reserved in affordable restaurants around Liverpool; dinner will be at participants’ expenses. Please sign up in the registration area if you plan to take part.

**Career discussion roundtables**
Monday 4 November, 13.15 – 14.15, Riverside Balcony

Are you assessing your career options? Join professionals from a range of sectors and professions for lunch to discuss different career paths and how to get into specific professions. Places are limited to nine participants per table so make sure you sign up early in the registration area.

Please note that a dedicated lunch for those interested in surgical research is taking place in room 4B at the same time. Places are limited so make sure you also sign up early in the registration area for this.

**Exhibition hall, jobs board and posters**
From 18.00 on Sunday 3 November for all refreshments and meals, until 16.20 on Tuesday 5 November, Hall 2

See the newest initiatives, as well as some of the best products and services available to cancer research professionals in the exhibit hall, and talk to expert staff about your needs.

The exhibit hall is the place to meet fellow participants: all meals and poster sessions will take place in the hall, and a jobs’ board will be available.

**Conference dinner (ticketed event)**
20.00 onwards, Tuesday 5 November, The Echo Arena, BT Convention Centre

This is a chance for you to relax and another opportunity to connect with fellow participants on the last evening of the Conference. At time of print, limited tickets were available for this event – please enquire at the payments desk in the registration area.
Cancer is a worldwide problem and therefore requires a worldwide effort if we want to make real progress. That is why AICR (Association for International Cancer Research) has no geographical boundaries and we fund the best cancer research proposals we receive, regardless of where in the world the projects are carried out.

**AICR is the leading charity dedicated to funding cancer research around the world.**

Future improvements in the diagnosis, treatment and prevention of cancer depend on more research being carried out today.

Thanks to the generosity and goodwill of the public over the last 32 years we have supported over 1600 cancer research projects in 32 different countries at a cost of over £173 million.

**Research Projects**

- 2 grant rounds per year – April & October
- Support for a project grant is typically 3 years, but 2 year, and 1 year pilot studies are also considered
- Proposals must be on basic or translational cancer research

[www.aicr.org.uk/research](http://www.aicr.org.uk/research)
Redefining cancer, redefining our solutions, restoring patients’ lives

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Find out more at astrazeneca.com/research
Programme at a glance

Workshops

14.00 – 15.00 Spreading the word – Communicating about cancer research in the media
Room 3A

Hosted by Kat Arney, Cancer Research UK, London, UK

Welcome address

15.20 – 15.30 Introduction from the Chair of the NCRI
Hall 1A Harpal S Kumar, Chair of the National Cancer Research Institute

Plenary lecture

Chaired by Gerard Evan, University of Cambridge, UK
15.30 – 16.10 Title TBC
Hall 1A Neal Rosen, Memorial Sloan-Kettering Cancer Center, New York, USA

Networking and refreshment break

16.10 – 16.40 Registration area and Galleria

Plenary lectures

Chaired by Herbie Newell, Northern Institute for Cancer Research, Newcastle upon Tyne, UK
16.40 – 17.20 Cervical cancer – problem solved?
Hall 1A Peter Sasieni, Wolfson Institute of Preventive Medicine, Queen Mary University, London, UK
17.20 – 18.00 The biology and clinical exploitation of BRAF and RAS signalling in cancer
Hall 1A Richard Marais, Cancer Research UK Manchester Institute, UK

Workshops

18.00 – 19.30 Panel debate: Prevention of breast cancer
Room 3A
Hosted by Breakthrough Breast Cancer

18.00 – 21.00 Bench to bedside for radiopharmaceutical trials: A road-map to navigate the regulatory challenges leading to successful delivery
Room 12
Hosted by Cancer Research UK, ECMC and UK Radiopharmacy Group Taskforce

Opening reception, networking and exhibition viewing

18.00 – 20.00 Light supper and refreshments will be served
Hall 2
Cervical cancer – problem solved?
Peter Sasieni
Wolfson Institute of Preventive Medicine, Queen Mary University, London, UK
16.40 – 17.20, Hall 1A

There have been a number of real breakthroughs in cervical cancer prevention over the last century, but as Mark Twain might have said, “Reports of the eradication of cervical cancer have been greatly exaggerated”.

I will review advantages and limitations of conventional cervical screening (Pap tests), human papillomavirus (HPV) testing, and HPV vaccination in the control of cervical cancer.

As technologies improve, we need to consider how best to minimise the harms and costs of intervention as well as trying to prevent this cancer. This talk will touch on a number of issues including:

• The effectiveness of conventional cervical screening and why cervical cancer is still the number one female cancer in many countries.
• The potential for improving cervical screening using HPV testing.
• The benefits and harms of starting cervical screening at 20 rather than 25.
• The appropriate upper age for cervical screening.
• The association between treatment for screen-detected disease and subsequent pre-term deliveries in pregnancy.

Finally I will consider how cervical cancer prevention might look 20 years from now.

The biology and clinical exploitation of BRAF and RAS signalling in cancer
Richard Marais
Cancer Research UK Manchester Institute, UK
17.20 – 18.00, Hall 1A

The protein kinase BRAF is mutated in about half of melanomas and its upstream activator, NRAS, is mutated in a further 20% of cases. To investigate the role of these proteins in melanomagenesis, we have developed mouse models of melanoma driven by V600E BRAF and G12D NRAS. Notably, when V600E BRAF is expressed in the melanocytes of mature mice, it induces BRAF in about 70% of the animals with a median latency of ~12 months. This shows that BRAF can be a founder mutation in melanoma, but the long latency suggests that other genetic events are required to cooperate with BRAF to drive melanomagenesis and we are currently examining gene-gene and gene-environmental relationships in this model to identify these additional events.

In contrast to V600E BRAF, G12D NRAS does not induce melanoma when expressed in adult mouse melanocytes. However, when expressed in the melanocytes of embryonic mice G12D NRAS induces leptomeningeal melanocytosis that presents the cardinal features of this rare disease in children, a condition that also appears to be driven by oncogenic RAS. We are currently investigating why congenital expression of oncogenic NRAS predisposes children to melanoma of the CNS.

Finally, BRAF has been validated as a therapeutic target in melanoma, but responses to BRAF drugs are limited and most patients will develop resistance after a relatively short period in remission. To investigate mechanisms of resistance, we are developing patient-derived xenografts from melanoma patients treated with targeted agents. These tumours will be fully characterised using next generation sequencing, proteomics and molecular pathology to allow us to determine mechanisms of resistance and establish a platform of precision medicine that will improve outcomes for melanoma patients.
Workshops

Spreading the word – Communicating about cancer research in the media
Hosted by Kat Arney
Cancer Research UK, London, UK
14.00 – 15.00, Room 3A

We live in an increasingly media-savvy world where stories can spread round the globe in a matter of minutes. From the perspective of cancer researchers, funders and healthcare providers, it’s vital that accurate, understandable information about cancer gets out to the public – whether it’s progress in research, improvements in treatment and survival, or information about risks and prevention. But how does this happen, and what can you do to help? In this session, aimed at researchers, medical professionals and research-funding organisations, we’ll be exploring how cancer stories make their way from the pages of academic journals into traditional and online media, and how Cancer Research UK’s science media team helps to achieve this. We’ll also provide tips and tricks on how to effectively engage with the media and wider public about your research, and discuss some of the issues and benefits involved.

Panel debate: Prevention of breast cancer
Hosted by Breakthrough Breast Cancer
18.00 – 19.30, Room 3A

50,000 women will be diagnosed with breast cancer this year. As things stand, these numbers are only set to rise, with current forecasts predicting 60,000 new breast cancer cases a year by 2030. Such shocking statistics make it clear that breast cancer prevention must become a priority for the research community and policy makers.

Encouragingly, the recently updated NICE guidelines on familial breast cancer signal a shift in focus from treating the disease to predicting and preventing it. But how will we maintain momentum in breast cancer prevention? What are the next steps in reducing disease incidence? Which year will see fewer cases of breast cancer cases recorded than the year before it? This debate will address these questions through interactive discussion between the panel members and the audience.

Panel:
Gareth Evans (Chair), The University of Manchester, UK
Tim Key, University of Oxford, UK
Tony Howell. The University of Manchester, UK
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Programme at a glance

Workshops
08.00 – 08.45  BACR educational workshop: Academic cancer drug discovery – Integrating chemistry and biology
  Room 11  Hosted by Michelle D Garrett and Ian Collins, The Institute of Cancer Research, London, UK
08.00 – 08.45  A beginner’s guide to targeted cancer treatments
  Room 3A  Hosted by Elaine Vickers, Science Communicated, Sheffield, UK

Introduction to the programme
08.50 – 09.00  Message from the Chair of the Scientific Committee
  Hall 1A  Gerard Evan, University of Cambridge, UK

Plenary lectures
Chaired by Caroline Dive, Cancer Research UK Manchester Institute, UK
09.00 – 09.40  Chromosomal instability and hopeful monsters: A driving force for cancer heterogeneity and evolution
  Hall 1A  Charles Swanton, Cancer Research UK London Research Institute and University College London Cancer Institute, UK
09.40 – 10.20  Inflammation and cancer: Reprogramming the immune microenvironment as an anti-cancer therapeutic strategy
  Hall 1A  Lisa M Coussens, Knight Cancer Institute, Oregon Health & Sciences University, Portland, USA

Poster session A (odd numbers), refreshment break, networking and exhibition viewing
10.20 – 11.20  For further details, please refer to the Poster Abstracts book or USB stick, and the exhibition section in this book
  Hall 2

Symposia
11.20 – 12.50  From functional genomics to executable cancer biology
  Room 11  Hosted by Jasmin Fisher, Microsoft Research Cambridge and University of Cambridge, UK
11.20 – 12.50  New methods for tumour functional imaging
  Room 3A  Hosted by Kevin Brindle, University of Cambridge and Cancer Research UK Cambridge Institute, UK
11.20 – 12.50  Debate: Continued development of therapies targeting oncogenic drivers is the biggest research priority in cancer medicine
  Hall 1A  Hosted by Gerard Evan, University of Cambridge, UK
11.20 – 12.50  Treatment-induced pain in cancer patients

conference.ncri.org.uk
Networking, exhibition viewing, poster viewing and lunch
12.50 – 13.50 For further details, please refer to the Poster Abstracts book or USB stick, and the exhibition section in this book
Hall 2

Commercial workshop
13.00 – 14.00 Biosimilar Monoclonal Antibodies: BioLogical Confidence
Room 12 Hosted by Hospira UK Limited
Lunch will be provided in the room

Poster session A (even numbers)
13.30 – 14.30 For further details, please refer to the Poster Abstracts book or USB stick, and the exhibition section in this book
Hall 2

Proffered paper sessions
14.30 – 16.00 Biomarkers
Room 3A Hosted by Nic Jones, Manchester Cancer Research Centre, The University of Manchester, UK
14.30 – 16.00 The cancer cell and model systems I
Room 11 Hosted by Caroline Dive, Cancer Research UK Manchester Institute, UK
14.30 – 16.00 Clinical trials
Hall 1A Hosted by Ricky Sharma, Gray Institute for Radiation Oncology & Biology and Oxford University Hospitals NHS Trust, UK
14.30 – 16.00 Treatment decision making, screening and palliative care
Hall 1B Hosted by Jane Seymour, University of Nottingham, UK

Workshops
14.30 – 16.00 A researcher’s guide to accessing high quality biosamples
Hall 1C Hosted by The Confederation of Cancer Biobanks
14.30 – 16.00 Brain cancer in teenagers and young adults
Room 3B Hosted by Colin Watts, University of Cambridge, UK
14.30 – 16.00 Developing trials with surgeons
Room 4 Hosted by Nigel Bundred, The University of Manchester, UK

Networking, exhibition viewing, poster viewing and refreshment break
16.00 – 16.20 For further details, please refer to the Poster Abstracts book or USB stick, and the exhibition section in this book
Hall 2
Programme at a glance

Parallel sessions

16.20 – 17.50  Life-altering late effects and their management in survivors of childhood malignancy
   Hall 1C
   Hosted by Rod Skinner, Great North Children’s Hospital and Royal Victoria Infirmary, Newcastle upon Tyne, UK

16.20 – 17.50  Molecular stratification and clinical management of adult high-grade glioma
   Hall 1B
   Hosted by Colin Watts, University of Cambridge, UK

16.20 – 17.50  ‘Real world’ data: Opportunities and challenges
   Room 11
   Hosted by David Ford, Swansea University, UK

16.20 – 17.50  Re-shaping clinical practice in neuroendocrine tumours (NETs)
   Room 3A
   Hosted by John Primrose, University of Southampton, UK and Juan Valle, The Christie NHS Foundation Trust, Manchester, UK

16.20 – 17.50  Smarter surgery for better cancer outcomes
   Room 3B
   Hosted by Dion Morton, University of Birmingham, UK

16.20 – 17.50  Targeting the epigenome
   Hall 1A
   Hosted by Robert Brown, Imperial College London, UK

16.20 – 17.50  The issues with tissues
   Room 4
   Hosted by Mairead MacKenzie, Independent Cancer Patients’, Voice, UK

Networking and break

17.50 – 18.00  Registration area

Prize awards

18.00 – 18.15  Cancer Research UK Prize ceremony
   Presented by Harpal S Kumar, Cancer Research UK

Plenary lecture

Chaired by Nic Jones, Chair of the Cancer Research UK Prizes Selection Panel

18.15 – 18.55  Cancer Research UK Lifetime Achievement Award
   Hall 1A
   winner – Polygenic susceptibility: What might it tell us?
   Bruce Ponder, Cancer Research UK Cambridge Institute, UK

Drinks reception, networking and exhibition viewing

18.55 – 20.45  For further details, please refer to the Poster Abstracts book
   or USB stick, and the exhibition section in this book
   Canapés and drinks will be provided
Workshop
19.00 – 20.15  
Room 3A  
Opportunities, challenges and funding your research:  
‘What should the future shape of biomarker driven clinical research look like?’

Hosted by GlaxoSmithKline

Light supper will be provided in the room

Chairs’ evening (by invitation)
20.00 – 22.30  
Grace Suite, The Hilton Liverpool
Plenary abstracts

Chromosomal instability and hopeful monsters: A driving force for cancer heterogeneity and evolution
Charles Swanton
Cancer Research UK London Research Institute and University College London Cancer Institute, UK
09.00 – 09.40, Hall 1A

Extensive evidence over the last four decades has demonstrated that two fundamental principles of Darwinian evolution are likely to operate within solid tumours, diversity and natural selection. Extensive somatic mutational heterogeneity has been described within solid tumours, with evidence of spatial intratumour heterogeneity emerging in most solid tumours. Recurrent mutations in driver genes between tumours of the same subtype and parallel evolution of subclones within the same tumour, where inactivation of the same tumour suppressor gene may occur across spatially separated regions provides further evidence of natural selection occurring within a patient’s lifetime.

Modern Darwinian views of evolution assert that evolutionary change is gradual and continuous. However, such gradualist views of evolution have had their detractors. Goldschmidt argued that discontinuous variation or macromutation might give rise to new species, whilst emphasising that most macromutations would have disastrous consequences on the organism, resulting in ‘monsters’. However, he argued that rarely a ‘macromutation’ may give rise to a new form of life, coining the phrase ‘hopeful monster’.

Cancer chromosomal instability can be considered a macromutational event, generating large leaps in phenotypic and adaptive change in daughter cells. In this talk both gradualist and macromutational views on cancer evolution will be highlighted. The role of tetraploidy and chromosomal instability in initiating such macromutational events in human tumours together with genetic mechanisms contributing to chromosomal instability and intratumour heterogeneity will be discussed.

Inflammation and cancer: Reprogramming the immune microenvironment as an anti-cancer therapeutic strategy
Lisa M Coussens
Knight Cancer Institute, Oregon Health & Sciences University, Portland, USA
09.40 – 10.20, Hall 1A

The concept that leukocytes are components of malignant tumours is not new; however, their functional involvement as promoting forces in tumour progression has only recently been appreciated. We are interested in understanding the molecular mechanisms that regulate leukocyte recruitment into neoplastic tissue, subsequent regulation those leukocytes exert on evolving cancer cells, and how malignant cells in turn respond to cytotoxic therapies. By studying transgenic mouse models of skin, lung, breast and pancreas cancer development, we have appreciated that adaptive leukocytes differentially regulate myeloid cell recruitment, activation, and behaviour, by organ-dependent mechanisms. In turn, selective myeloid cell types provide key survival factors to malignant cells, foster angiogenic programs and invariably blunt CD8+ T cell-mediated killing of tumour cells. Treatment of transgenic mice predisposed to these various cancer types with agents that selectively block adaptive/myeloid-based programmes results in slowing of primary tumour growth, improved responses to chemotherapeutic drugs, and significantly diminished presence of metastatic disease. To be presented will be recent insights into organ and tissue-specific regulation of epithelial cancer development by adaptive and innate immune cells, and new studies evaluating how attenuating pro-tumour properties of myeloid cells can be exploited to enhance therapeutic responses to cytotoxic therapy.

Lisa M Coussens acknowledges generous support from the NIH/NCI, the Department of Defense Era of Hope Scholar Expansion Award, Susan G Komen Foundation, and the Breast Cancer Research Foundation.
Cancer Research UK Lifetime Achievement Award winner – Polygenic susceptibility: What might it tell us?
Bruce Ponder
Cancer Research UK Cambridge Institute, UK
18.15 – 18.55, Hall 1A

Although trained in medical oncology and Head of an Oncology Department, my focus has always been the hope that better understanding of cancer development, and of genetic susceptibility, might open the way to interventions at an earlier stage. After a PhD on the molecular structure of chromatin, I developed in the late 1970s parallel research programmes in the clonal organisation of epithelia and in genetic predisposition to cancer, each as a way to understanding mechanisms. I will describe some of the results and the lessons learned along the way. I will review the current challenges as I see them, and speculate on how my own and other current work on common genetic variation might (possibly) contribute to my original goal of earlier intervention. For the past 17 years, much of my attention has been on helping to build the new cancer centre and institute in Cambridge. If time permits, I will reflect also on some of the lessons that I have learned from this.
Symposia

From functional genomics to executable cancer biology

Room 11  Hosted by Jasmin Fisher, Microsoft Research Cambridge and University of Cambridge, UK
11.20 – 11.25  Introduction by the host
11.25 – 11.50  Transcriptional network control of normal and leukaemic blood stem/progenitor cells
  Bertie Gottgens, University of Cambridge, UK
11.50 – 12.15  Computational models to predict and dissect mechanistically drug sensitivity in cancer
  Julio Saez Rodriguez, European Bioinformatics Institute (EMBL-EBI), Cambridge, UK
12.15 – 12.40  Can computation help cure cancer?
  Jasmin Fisher, Microsoft Research Cambridge and University of Cambridge, UK
12.40 – 12.50  Discussion

New methods for tumour functional imaging

Room 3A  Hosted by Kevin Brindle, University of Cambridge and Cancer Research UK Cambridge Institute, UK
11.20 – 11.25  Introduction by the host
11.25 – 11.50  Title TBC
  Bernd Pichler, University of Tuebingen, Germany
11.50 – 12.15  Title TBC
  Sarah Nelson, University of California San Francisco, USA
12.15 – 12.40  Illuminating cancer biology with optoacoustic and thermoacoustic imaging
  Vasilis Ntziachristos, Helmholtz Zentrum München and Technische Universität München, Germany
12.40 – 12.50  Discussion

Debate: Continued development of therapies targeting oncogenic drivers is the biggest research priority in cancer medicine

Hall 1A  Hosted by Gerard Evan, University of Cambridge, UK
11.20 – 12.50  Speakers to include Charles Swanton¹ and James Larkin²
  ¹Cancer Research UK London Research Institute and University College London Cancer Institute, UK; ²The Royal Marsden NHS Foundation Trust, London, UK

Treatment-induced pain in cancer patients

Room 3B  Hosted by Michael Bennett, University of Leeds, UK
11.20 – 11.25  Introduction by the host
11.25 – 11.50  Treatment-induced pain in cancer patients
Patrick Dougherty, The University of Texas MD Anderson Cancer Center, Houston, USA

11.50 – 12.15  Update on targeted treatments for painful neuropathy
Marie Fallon, Edinburgh Cancer Research Centre (IGMM) and Western General Hospital, Edinburgh, UK

12.15 – 12.40  Epidemiology and risk factors for persistent pain after breast cancer surgery
Julie Bruce, University of Warwick, UK

12.40 – 12.50  Discussion
From functional genomics to executable cancer biology

Introduction
Jasmin Fisher
Microsoft Research Cambridge and University of Cambridge, UK
11.20 – 11.25, Room 11

The aim of this session is to present the ‘next wave’ of computational methods for cancer biology. The session will cover recent advances in functional genomics to assemble molecular network models, and how these provide the foundations for dynamic mathematical models and discrete models of stem cell differentiation. The session is intended for the curious cancer biologist, who is eager to learn new ways to boost the traditions in experimental biology, and challenge the staggering complexity observed in biological systems.

Transcriptional network control of normal and leukaemic blood stem/progenitor cells
Bertie Gottgens
University of Cambridge, UK
11.25 – 11.50, Room 11

The transcriptional control of blood stem cells is critical for their normal function, and a large number of leukaemias arise when this fine balance of gene activities is disturbed. Transcription factors generally function as components of wider regulatory networks. Our group uses a combination of experimental and computational approaches to study transcriptional regulatory networks in blood stem cells; to discover how transcription factor networks control the function of blood stem cells; and to identify how perturbations of such networks can cause leukaemia. We are addressing these issues using computational analysis coupled with single cell gene expression studies, genome-scale analysis of transcription factor binding sites, and transgenic mouse assays. During my talk, I will provide an overview of the nature of our new data, and outline how they raise several fundamental questions concerning the functionality of transcription factor binding events and the dynamic nature of cross-regulatory relationships in both normal and malignant cells.

Computational models to predict and dissect mechanistically drug sensitivity in cancer
Julio Saez Rodriguez
European Bioinformatics Institute (EMBL-EBI), Cambridge, UK
11.50 – 12.15, Room 11

Predicting the response of a patient to a therapy is a major goal in modern oncology and a requisite to develop a personalised treatment. To model the heterogeneous response of patients to treatment, high-throughput screenings of therapeutic compounds against a panel of heterogeneous cancer cell lines have been performed. These studies have unveiled multiple relationships between genomic alterations and drug responses. Various computational approaches have been proposed to predict sensitivity based on genomic features, while others have used the chemical properties of the drugs to ascertain their effect. In an effort to integrate these complementary approaches, we have developed machine learning models to predict the response of cancer cell lines to drug treatment based on both the genomic features of the cell lines and the chemical properties of the considered drugs. Genomic data is integrated with various sources of prior knowledge whenever possible. These computational models can be used to optimise the experimental design of drug-cell screenings as well as to screen \textit{in silico} novel compounds, thus identifying novel new drug repositioning opportunities. They also point at molecular processes involved in resistance mechanisms, thus proposing systems to analyse in a mechanistic fashion. These mechanisms can then be characterised in detail using pathway models. Specifically, we build
Can computation help cure cancer?

Jasmin Fisher
Microsoft Research Cambridge and University of Cambridge, UK
12.15 – 12.40, Room 11

Computational modelling is rapidly developing into a cornerstone of biomedical research, driven by the need to integrate highly complex multidimensional data and its potential to reveal underlying mechanistic principles. ‘Executable biology’ is a pioneering approach focused on the design of executable computer programs that recapitulate biological phenomena. While traditional mechanistic models in biology are usually described by diagrams (giving a fairly static picture of cellular processes), executable biology seeks to translate such static diagrams into dynamic models using formal computational methods that were originally designed for the construction and analysis of complex man-made systems (i.e. computers and computer programs). In this talk I will survey some of the modelling efforts in this direction, and emphasise the applicability and benefits of executable models in cancer research. I will conclude with a call for a mind shift, arguing that a new, cross-disciplinary approach, using computer modelling and formal verification is needed to systematically identify the causes of cancers and the ‘program’ of life. I suggest that only such an approach can help us cure and control cancer, and highlight some of the major challenges that executable biology poses for biological and medical research.

Discussion
12.40 – 12.50

New methods for tumour functional imaging

Introduction
Kevin Brindle
University of Cambridge and Cancer Research UK Cambridge Institute, UK
11.20 – 11.25, Room 3A

Imaging aspects of tumour biology in the cancer patient can be used for tumour detection, grading and monitoring of treatment response. This session, which should be of interest to both basic scientists and clinicians, will describe new functional imaging methods that have recently been introduced into the clinic. These include hybrid positron emission tomography/magnetic resonance imaging (PET/MRI), MR imaging with hyperpolarised 13C-labelled cell substrates, and photoacoustic and intraoperative fluorescence imaging.

Title TBC
Bernd Pichler
University of Tuebingen, Germany
11.25 – 11.50, Room 3A
Symposia abstracts

Title TBC
Sarah Nelson
University of California San Francisco, USA
11.50 – 12.15, Room 3A

Illuminating cancer biology with optoacoustic and thermoacoustic imaging
Vasilis Ntziachristos
Helmholtz Zentrum München and Technische Universität München, Germany
12.15 – 12.40, Room 3A

Optical imaging is unequivocally the most versatile and widely used visualisation modality in the life sciences. Yet it is significantly limited by photon scattering, which complicates imaging beyond a few hundred microns. For the past few years however, there has been an emergence of powerful new imaging methods that can offer high resolution imaging beyond the penetration limits of microscopic methods. These methods can prove essential in cancer research. Of particular importance is the development of multi-spectral opto-acoustic tomography (MSOT) that brings unprecedented optical imaging performance in visualising anatomical, physiological and molecular imaging biomarkers. Some of the attractive features of the method are the ability to offer 10–100 microns resolution through several millimetres to centimetres of tissue and real-time imaging. In parallel we have now achieved the clinical translation of targeted fluorescent probes, which opens new ways in the interventional detection of cancer in surgical and endoscopy optical molecular imaging. This talk describes current progress with methods and applications for in vivo optical, opto-acoustic and thermoacoustic imaging in cancer and outlines how new opto-acoustic and fluorescence imaging concepts are necessary for accurate and quantitative molecular investigations in tissues.

Discussion
12.40 – 12.50

Debate: Continued development of therapies targeting oncogenic drivers is the biggest research priority in cancer medicine

Introduction
Gerard Evan
University of Cambridge, UK
11.20 – 12.50, Hall 1A

Speakers to include Charles Swanton¹ and James Larkin²
¹Cancer Research UK London Research Institute and University College London Cancer Institute, UK; ²The Royal Marsden NHS Foundation Trust, London, UK
Treatment-induced pain in cancer patients

Introduction
Michael Bennett
University of Leeds, UK
11.20 – 11.25, Room 3B

This symposium will explore pain in cancer patients that results from treatment, specifically from chemotherapy and surgery. The expert speakers will discuss basic mechanisms on chemotherapy induced neuropathic pain, translational work on targeted treatments, and finally the prevalence and epidemiology of post-breast cancer surgery pain. The symposium will be of relevance to basic scientists, as well as medical and nursing clinicians.

Treatment-induced pain in cancer patients
Patrick Dougherty
The University of Texas MD Anderson Cancer Center, Houston, USA
11.25 – 11.50, Room 3B

In this symposium recent findings on a key patient risk factor for chemotherapy-induced peripheral neuropathy (CIPN) and new insights to the basic mechanisms garnered from pre-clinical studies will be presented.

Patients with chronic CIPN show depletion of skin innervation that parallels in magnitude the distribution of CIPN symptoms. Surprisingly, it was also discovered that there is a proximal to distal decrease in baseline innervation density in normal volunteers in a pattern that exactly matches that of symptoms in CIPN patients. These findings strongly suggest that baseline innervation density is a latent factor that can predict those at greatest risk for CIPN, and could be used to guide personalised treatment to avoid this complication. Data will be presented showing that patients with deficits in distal innervation density assessed using non-invasive imaging correlate to pre-treatment sensory deficits. Moreover, patients with pre-treatment sensory deficits go on to develop more spontaneous pain during chemotherapy than those who had normal sensory function.

Previous pre-clinical work has shown the involvement of an inflammatory response in CIPN. New data that will be presented in this symposium indicate that Toll-like receptor 4 (TLR4) is a key in triggering this response that leads to CIPN. TLR4 is shown to be expressed on neurons that innervate the skin and to become activated in animals treated with the chemotherapy drug paclitaxel. In addition, a TLR4 antagonist is shown to both reverse pre-established paclitaxel CIPN, and also to prevent its onset when given along with the chemotherapy drug. Even more exciting is that similar findings have been extended to the chemotherapeutics oxaliplatin and bortezomib. The findings here provide a simple unifying hypothesis for all these clinical conditions that could in turn result in a single shared medication for CIPN that would not interfere with the anti-tumour effects of the chemotherapy drugs.

Update on targeted treatments for painful neuropathy
Marie Fallon
Edinburgh Cancer Research Centre (IGMM) and Western General Hospital, Edinburgh, UK
11.50 – 12.15, Room 3B

In an attempt to alleviate painful chemotherapy induced peripheral neuropathy (CIPN), clinicians and patients try various therapeutic interventions, despite the limited evidence to support efficacy of these treatments. The rationale for such use is mostly based on the evidence for the treatment options in non-CIPN peripheral neuropathy syndromes, as this area is
more robustly studied than CIPN. It may be reasonable to extrapolate data in this way, however increasingly it is thought that underlying neurobiological changes dictate analgesic response rather than specific aetiology.

Antidepressants: Duloxetine is a serotonin-norepinephrine reuptake inhibitor (SNRI) with known efficacy in the treatment of various pain syndromes and there are three randomised controlled trials (RCTs) with positive results at 60mg per day in diabetic peripheral neuropathic pain. In CIPN, a pilot trial suggested some benefit for duloxetine. A 231 patient phase III RCT evaluated duloxetine at 60mg per day for the treatment of painful CIPN attributed to taxane or oxaliplatin therapy. Patients who received duloxetine had a larger average decrease in pain score and sub-group analysis supported the most benefit in patients who had received oxaliplatin with little or no benefit in patients who had received paclitaxel. There is low level evidence for the use of venlafaxine. An RCT with nortriptyline in a crossover design involving 51 patients with cisplatin induced peripheral neuropathy showed no significant effect.

Antiepileptics: The gabapentinoids - There are limited supporting data for the use of gabapentin to treat CIPN; furthermore a phase III randomised double-blind crossover trial with 115 patients failed to demonstrate any suggestion of benefit. There is low-level evidence for pregabalin with a single-blind study.

Opioids: Limited data are available for the use of opioids in the treatment of CIPN, however open studies suggest potential benefit.

Topical agents: Topical amitriptyline, ketamine +/- baclofen - an RCT involving 208 patients with CIPN from a variety of chemotherapeutic agents showed a greater improvement in the amitriptyline, ketamine, baclofen arm particularly in relation to sensory symptoms. Topical menthol - translational research with the TRPM8 agonist, menthol, in CIPN shows potential promised but needs further evaluation. High dose topical capsaicin patches (8%) are licensed for peripheral neuropathic pain and, with case series of patients with CIPN, are showing promise, however appropriately designed studies are awaited.

Other agents: Other potential treatments include acetyl-L-carnitine (ALC), acupuncture and neurostimulation.

**Epidemiology and risk factors for persistent pain after breast cancer surgery**

**Julie Bruce**

University of Warwick, UK

12.15 – 12.40, Room 3B

Chronic post-surgical pain (CPSP) is a well-recognised adverse event; half of women report pain persisting for 1 to 2 years after breast cancer surgery. Two-thirds of those with CPSP experience neuropathic pain, although few studies incorporate standardised neuropathic pain instruments. Less is known about those at greatest risk of adverse pain-related outcomes after cancer surgery. However, improving identification of risk subgroups will provide opportunities for targeting prevention and treatment.

This session presents a prospective cohort study that investigated the relative contribution of psychological, sociodemographic, perioperative and acute postoperative factors associated with painful symptoms at 4 and 9 months after breast cancer surgery. We recruited 362 women, with newly diagnosed histologically proven primary breast cancer, from four centres in Northern Scotland.

Data collection was undertaken before surgery, in the first week, 4 and 9 months postoperatively. We included standardised instruments to capture psychological distress and resilience, pain intensity, location and character. Nerve handling (division or preservation) of the intercostobrachial nerve was recorded intraoperatively.
At 4 and 9 months after surgery, incidence of chronic painful symptoms, not present preoperatively, was 68% and 63% respectively. Univariate analysis revealed that multiple psychological factors and nerve division was associated with chronic pain at 4 and 9 months. Independent predictors of CPSP at 4 months included younger age and acute postoperative pain, whereas preoperative psychological ‘robustness’, a composite variable comprising high dispositional optimism, high positive affect and low emotional distress, was protective. At 9 months, younger age, axillary node clearance and severity of acute postoperative pain were predictive of pain persistence. Of those reporting CPSP, a quarter experienced moderate to severe pain and 25% were positive on neuropathic instruments (DN4 and S-LANSS). A high proportion of women report painful symptoms, altered sensations and numbness, in the upper body within the first 9 months after resectional breast surgery and cancer treatment.

Discussion
12.40 – 12.50
BACR educational workshop: Academic cancer drug discovery – Integrating chemistry and biology

Hosted by Michelle D Garrett and Ian Collins, The Institute of Cancer Research, London, UK

08.00 – 08.45, Room 11

The integration of chemistry and biology is critical to the success of any cancer drug discovery project, whether based in a commercial or an academic organisation. We are interested in small molecule drug discovery, where the key challenge is to produce a molecule (chemistry) that can potentially kill or inhibit the growth of cancer cells in the human body (biology) and ultimately to demonstrate a benefit to patients in the clinic. The perspective provided in this workshop will highlight the opportunities and benefits of undertaking small molecule anticancer drug discovery in the academic setting. Importantly, we will emphasise how the productive interplay of chemistry and biology research can result in both useful drug molecules and new scientific discoveries, highlighting the role of high-quality chemical tool compounds.

We will consider typical scientific questions asked during the lifetime of a cancer drug discovery project, and illustrate some approaches available to academic laboratories to tackle these. Examples of the questions that arise include: What makes a good cancer drug target? What makes a useful chemical tool and how does it differ from a cancer drug candidate? How can we find chemical starting points for drug discovery? How can we define and follow the biological activity of our molecules and choose which to progress? What does chemical optimisation to generate a candidate drug involve? What opportunities for new biological research are presented during a drug discovery project? How can the understanding of cancer target biology change during the lifetime of a project?

We will illustrate approaches to answering the questions posed above with brief examples from our own research experience, and demonstrate that, when chemistry and biology are integrated together, answering these questions can lead to the identification of novel and effective drug molecules and also to new science.

A beginner’s guide to targeted cancer treatments

Hosted by Elaine Vickers, Science Communicated, Sheffield, UK

08.00 – 08.45, Room 3A

This workshop will provide nurses, patients and other non-scientists with an introduction to targeted cancer treatments and an explanation of key concepts and terminology.

There will be:

- An overview of the main targets of new treatments, including an introduction to growth factor receptors and their downstream pathways
- An introduction to monoclonal antibodies and kinase inhibitors, including:
  - How they work
  - How they’re made
  - How they compare with each other
- Insight into why everyone’s talking about the EMT, intratumoural heterogeneity, genetic instability and the tumour microenvironment
Commercial workshop: Biosimilar Monoclonal Antibodies: BioLogical Confidence

Hosted by Hospira UK Limited

13.00 – 14.00, Room 12

The workshop ‘Biosimilar Monoclonal Antibodies: BioLogical Confidence’ will provide a comprehensive review of biosimilar monoclonal antibodies whilst objectively presenting and addressing the challenges and issues relating to this exciting and rapidly evolving area. You will hear about the science and latest technological advances in biosimilar development and production. In addition, areas such as the stringent quality standards required in the manufacturing process and the robust regulatory environment in respect of efficacy, safety and comparability will all be reviewed. The interchangeability and uptake of biosimilars along with their potential health economic benefits will also be discussed.

This workshop is sponsored by Hospira. Hospira is one of the major companies producing and marketing biologics globally.

Peter Johnson (Chair), Cancer Research UK Centre, Southampton, UK

The changing world of therapeutic monoclonal antibody design

Martin Glennie, Cancer Research UK Centre, Southampton, UK

Biosimilar Monoclonal Antibodies: BioLogical Confidence

Paul Cornes, Bristol Haematology and Oncology Centre, Bristol, UK

Lunch will be provided in the room

A researcher’s guide to accessing high quality biosamples

Hosted by The Confederation of Cancer Biobanks

14.30 – 16.00, Hall 1C

Researchers often complain of lack of availability of high-quality biosamples for their research and research funders are still inundated with requests to fund the creation of new sample collections. However, thousands of biosamples for cancer research are already available and waiting to be accessed and many biobanks follow established, efficient methods for prospective collection of biosamples.

This workshop will provide guidance for researchers on where to find biosamples, how to access them and how to ensure they are fit for purpose. Tips on getting the most out of a relationship with a biobank and opening up access to existing sample collections will also be covered.

Andy Hall (Chair), University of Newcastle, UK

What are funders looking for in a project involving tissue?

Manuel Salto-Tellez, University of Belfast, UK

The challenges of working with tissue: pathology and red tape

Bridget Wilkins, St Thomas’ Hospital, London, UK

Finding biosamples – where do you start?

Ian Forgie, Tayside Tissue Bank, UK
Understanding sample quality
Anne Carter, National Cancer Research Institute, UK

Panel discussion

### Brain cancer in teenagers and young adults

**Hosted by Colin Watts,** University of Cambridge, UK

14.30 – 16.00, Room 3B

The aim of this session will be to highlight the urgent need to improve our understanding and awareness of brain cancer in the teenager and young adults (TYA) age group. This issue was raised at the last NCRI Brain Clinical Studies Group strategy meeting.

The session will begin with an overview of clinical trial recruitment and the need for international collaboration in these rare cancers. This will be followed by reviews of the spectrum of high-grade glioma and intracranial germ cell tumours with particular emphasis on the TYA population.

This session is targeted at both adult and paediatric oncologists, neuro-surgeons, specialist nurses and scientists. We hope that by raising awareness we can improve research and management of this neglected patient group.

### Developing trials with surgeons

**Hosted by Nigel Bundred,** The University of Manchester, UK

14.30 – 16.00, Room 4

This workshop will provide guidance on developing a trial with a surgical component. It is aimed at surgical and oncological trainees, but will benefit all current and aspiring trialists. Advice will be given on how to find and apply for funding to carry out research with a surgical component, including tips on what makes a successful application. The surgical collaboratives will be showcased as a trainee-led initiative that is growing a new generation of research active surgeons. Finally, a surgeon’s perspective on the best way to engage surgeons in developing and running clinical trials will be presented.

**Getting through peer review**

David Sebag-Montefiore, Chair of Cancer Research UK CTAAC Committee

How to find and apply for funding to carry out surgical research, with tips for a successful funding application.

**The collaborative experience**

Julie Cornish, University of Cardiff, UK, and Andy Torrance, University of Birmingham, UK

Recent trainee-led surgical trials and first-hand experience of the surgical research collaborative infrastructure.

**Engaging surgeons: For surgeons and oncologists**

Dion Morton, University of Birmingham, UK

How to engage surgeons in developing and running clinical trials.
Opportunities, challenges and funding your research: ‘What should the future shape of biomarker driven clinical research look like?’

Hosted by GlaxoSmithKline

19.00 – 20.15, Room 3A

This interactive session, chaired by Professor Sebag-Montefiore, will discuss the shared vision of individualised patient cancer care through the successful delivery of biomarker driven clinical research. Dr Simon Meadowcroft will discuss the aspirations underpinning the investment being made by GSK in this dynamic area of cancer research. Professor Tim Maughan, Chief Investigator for FOCUS 4, will present on the important challenges researchers face through such trial designs, and possible solutions. Funding and support opportunities offered by Cancer Research UK and the Medical Research Council around biomarker driven clinical research will be shared by Dr Kate Law, CRUK and Dr. Rhoswyn Walker, MRC; this will include ideas on how investigators may increase their chances of a successful funding request. The meeting will draw to a close following an interactive expert panel question and answer session, and we invite delegates to email questions for the panel discussion in advance of the meeting using this email address: Bhupinder.k.mann@gsk.com

David Sebag-Montefiore, Clinical Associate Professor/Honorary Consultant in Clinical Oncology, St James University Hospital Leeds and Chair, CTAAC Committee

Simon Meadowcroft, Oncology Medical Director, GlaxoSmithKline

Tim Maughan, Professor of Clinical Oncology, University of Oxford and Chair, NCRI Clinical and Translational Radiotherapy Research Working Group

Kate Law, Director of Clinical Research, Cancer Research UK

Rhoswyn Walker, Programme Manager for Cancer, Medical Research Council, UK

Light supper will be provided in the room
## Biomarkers

**Room 3A**  
Hosted by **Nic Jones**, Manchester Cancer Research Centre, The University of Manchester, UK

### 14.30 – 14.45

**AstraZeneca Student Prize Award: MicroRNA-135b promotes cancer progression acting as a downstream effector of oncogenic pathways in colon cancer**  
**Nicola Valeri**, Institute of Cancer Sciences, University of Glasgow, UK

### 14.45 – 14.55

**Evaluation of PIK3CA mutation as a predictor of benefit from NSAID therapy in colorectal cancer**  
**David Church**, The Wellcome Trust Centre for Human Genetics and Oxford Cancer Centre, University of Oxford, UK

### 14.55 – 15.05

**miR-21 down-regulates junctional adhesion molecule-A (JAM-A) during colorectal cancer progression**  
**Andrea Lampis**, Institute of Cancer Sciences, University of Glasgow, UK

### 15.05 – 15.15

**Deep analysis of signalling plasticity in a breast cancer kinase network during acquisition of resistance to PI3K and mTORC1/2 inhibitors**  
**Pedro Cutillas**, Barts Cancer Institute, Queen Mary University of London and MRC Clinical Sciences Centre, London, UK

### 15.15 – 15.25

**Pan-genomic analysis of hypoxic breast cancer reveals lncRNAs associated with clinicopathological features**  
**Hani Choudhry**, King Abdulaziz University, Jeddah, Saudi Arabia and The Wellcome Trust Centre for Human Genetics, University of Oxford, UK

### 15.25 – 15.35

**Volatile biomarkers discriminate between bronchial epithelial cells with distinct mutations**  
**Michael Davies**, University of Liverpool, UK

### 15.35 – 15.45

**CCP Score: A novel genetic test for prostate cancer**  
**Dan Berney**, Queen Mary, University of London, UK

### 15.45 – 16.00

**Discussion**

## The cancer cell and model systems I

**Room 11**  
Hosted by **Caroline Dive**, Cancer Research UK Manchester Institute, UK

### 14.30 – 14.45

**BACR AstraZeneca Frank Rose Award: The signalling networks regulating cell shape**  
**Chris Bakal**, The Institute of Cancer Research, London, UK
14.45 – 14.55 The Hippo pathway polarises the actin cytoskeleton during collective migration of Drosophila border cells
Ichha Khanal, Cancer Research UK London Research Institute, UK

14.55 – 15.05 NRIP1 drives tip-cell selection downstream of Notch signaling by inhibiting ALK5 activation
Irene Maria Aspalter, Cancer Research UK London Research Institute, UK

15.05 – 15.15 Tetraploidy is permissive for chromosomal instability and accelerates cancer genome evolution
Sally Dewhurst, Cancer Research UK London Research Institute and University College London Cancer Institute, UK

15.15 – 15.25 Lineage tracing reveals the cellular basis of early metastasis in oesophageal squamous carcinoma
Philip Jones, MRC Cancer Cell Unit, Cambridge, UK

15.25 – 15.40 BACR Translational Research Award: Monitoring the cancer genome in plasma using circulating tumour DNA
Nitzan Rosenfeld, Cancer Research UK Cambridge Institute, University of Cambridge, UK

15.40 – 16.00 Discussion

Clinical trials

14.30 – 14.40 Clinical outcomes in patients with castrate-refractory prostate cancer (CRPC) metastatic to bone randomised in the factorial TRAPEZE trial to docetaxel (D) with strontium-89 (Sr89), zoledronic acid (ZA), neither or both
Nick James, University of Birmingham, UK

14.40 – 14.50 A polyphenol rich whole food supplement slows PSA progression in men with prostate cancer: A double-blind, placebo-controlled randomised trial - The NCRN Pomi-T study
Robert Thomas, Bedford Hospital and Cranfield University, Bedford, UK

14.50 – 15.00 The DietComplLyf study: A prospective cohort study of breast cancer survival and phytoestrogen consumption
Ruth Swann, University of Westminster, London, UK
Proffered paper sessions

15.00 – 15.10  Adjuvant Tamoxifen To offer more? (aTTom) - a randomised comparison of continuing adjuvant tamoxifen to 10 years compared to stopping after 5 years among 6953 women with ER positive or ER untested early breast cancer: Overall and subgroup findings.
    Daniel Rea, University of Birmingham, UK

15.10 – 15.20  PETROC / OV21 Randomised phase II/III Trial of PEritoneal Treatment for Ovarian Cancer: Initial results of the phase II study in preparation for extension to phase III. A collaborative trial of the NCRI, NCIC, GEICO, and SWOG Gynaecological Cancer Study Groups
    Chris Gallagher, St Bartholomew’s Hospital, London, UK

15.20 – 15.30  A randomised trial of 72 hour infusional bleomycin in BEP (cisplatin, etoposide and bleomycin) versus conventional weekly bleomycin in patients with metastatic IGCCCG good prognosis disease
    Jonathan Shamash, Barts Cancer Institute, London, UK

15.30 – 15.40  Identification of plasma metabolite changes following phosphatidylinositol-3-kinase (PI3K) inhibition with GDC-0941, a potent and selective pan-Class I inhibitor of PI3K: Preclinical discovery followed by clinical qualification in a Phase I clinical trial
    Florence Raynaud, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK

15.40 – 15.50  Tumour- and treatment-related colostomy rates following 5Fluorouracil (5FU) and Mitomycin (MMC) or 5FU and Cisplatin (Cisp) chemoradiation (CRT) with or without maintenance chemotherapy in squamous cell carcinoma of the anus: Results of the randomised phase III trial ACT II
    Rob Glynne-Jones, Mount Vernon Centre for Cancer Treatment, Northwood, UK

15.50 – 16.00  Discussion

Treatment decision making, screening and palliative care

Hall 1B  Hosted by Jane Seymour, University of Nottingham, UK

    Kate Fife, Addenbrooke’s Hospital, Cambridge, UK
14.40 – 14.50  Results from the UNBIASED study (UK - Netherlands - Belgium International SEDation study): Reported practices of physicians and nurses in three European countries
   Jane Seymour, University of Nottingham, UK

14.50 – 15.00  An all-Ireland population-based study of past and current physical and psychological side-effects following prostate cancer treatments
   Lesley Anderson, Queen’s University Belfast, UK

15.00 – 15.10  Reduction in interval cancer rates following the introduction of two-view mammography in the UK breast screening programme
   Amanda Dibden, Queen Mary, University of London, UK

15.10 – 15.20  Clinical implications of a prostate cancer risk SNP profile in 2 treatment cohorts
   Chee Goh, The Institute of Cancer Research, London, UK

15.20 – 15.30  Over or under treatment? A systematic review and meta-analysis of factors determining change of management in active surveillance for localised prostate cancer
   Andrew Simpkin, University of Bristol, UK

15.30 – 15.40  Obesity and the outcome of young breast cancer patients in the UK: The POSH study
   Ellen Copson, University of Southampton, UK

15.40 – 16.00  Discussion
Proffered paper session abstracts

Biomarkers

Hosted by Nic Jones, Manchester Cancer Research Centre, The University of Manchester, UK

AstraZeneca Student Prize Award: MicroRNA-135b promotes cancer progression acting as a downstream effector of oncogenic pathways in colon cancer

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14.30 – 14.45, Room 3A

Background

microRNAs (miRs) are small non-coding RNAs often deregulated in colorectal cancer (CRC). Our study aimed at identifying miRs with a driver role in carcinogenesis altered by similar mechanisms in both human and mouse CRC.

Goal of the study was to use CRC mouse models for the pre-clinical development of anti-miRs as therapeutics.

Method

Azoximetane (AOM)/Dextran-Sulfate (DSS) treated mice or CDX2P-NLS Cre;Apc¹⁸⁶⁷⁸ (CPC;Apc) mice were used to study inflammation-associated and sporadic APC related CRC respectively. Human Inflammatory Bowel Disease associated (n=45), and sporadic (n=62) CRC with their matched normal tissues were used for miR expression analysis. miR and gene expression profiling was assessed by nCounter technology. Anti-miR-135b probes for in vivo studies were synthesized by Girindus.

Results

miR profiling from AOM/DSS and CPC;Apc CRC revealed that miR-135b is one of the most up-regulated miR in both models. MiR-135b was over-expressed in human IBD and sporadic CRC and was associated with poor survival. Molecular studies in mouse embryo fibroblast, human CRC cell lines and tumour derived organoids defined APC/β-Catenin and SRC-PI3K as key pathways in miR-135b activation. MiR-135b up-regulation resulted in reduced apoptosis and increased cell growth due to the down-regulation of TGFRB2, DAPK1, APC and FIH. MiR-135b silencing in vivo reduced tumour multiplicity and tumour load in the AOM/DSS CRC model. Mice treated with anti-miR-135b showed well-differentiated tumours with acinar pattern while tumours in the control groups showed poor differentiation and adenomatous pattern. Tumours in mice treated with anti-miR-135b showed reduced proliferation and increased apoptosis.

Conclusion

Our data suggest that miR-135b is a key molecule whose activation is downstream of driver genes frequently mutated in CRC. The “in vivo” silencing of miR-135 shows preclinical efficacy with low toxicity and represents the first in vivo study for the use of anti-miRs in CRC treatment.

Evaluation of PIK3CA mutation as a predictor of benefit from NSAID therapy in colorectal cancer

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14.45 – 14.55, Room 3A

Background
Aspirin and other NSAIDs protect against colorectal cancer (CRC) and are associated with reduced disease recurrence and improved outcome following primary treatment. However, toxicities of NSAIDs have limited their use as antineoplastic therapy. Recent data have suggested that the benefit of aspirin after CRC diagnosis is limited to patients with PIK3CA-mutant cancers. We sought to determine the predictive utility of PIK3CA mutation for benefit from both COX-2 inhibition and aspirin.

Method
We performed molecular analysis of tumours from 896 participants in VICTOR, a large randomized trial comparing rofecoxib with placebo following primary CRC resection. We compared relapse-free survival (RFS) and overall survival (OS) between rofecoxib therapy and placebo, and between the use and non-use of low-dose aspirin, according to tumour PIK3CA mutation status.

Results
We found no evidence of a greater benefit from rofecoxib treatment compared to placebo in patients whose tumour had PIK3CA mutation (multivariate adjusted hazard ratio [HR]; 1.2, 95% CI 0.53-2.72; P=0.66; P_INTERACTION=0.47), compared with PIK3CA wild-type cancers (HR 0.87; 95% CI 0.64-1.16; P=0.34). In contrast, regular aspirin use after CRC diagnosis was associated with a reduced rate of CRC recurrence in patients with PIK3CA-mutant cancers (HR 0.11; 95% CI 0.001 to 0.832; P=0.027; P_INTERACTION=0.024), but not in cases lacking tumour PIK3CA mutation (HR 0.92; 95% CI 0.60-1.42; P=0.71).

Conclusion
Although tumour PIK3CA mutation does not predict benefit from rofecoxib treatment, it merits further evaluation as a predictive biomarker for aspirin therapy. Our findings are concordant with recent data, and support the prospective investigation of adjuvant aspirin in PIK3CA-mutant CRC.

miR-21 down-regulates Junctional Adhesion Molecule-A (JAM-A) during colorectal cancer progression
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14.55 – 15.05, Room 3A

Background
MicroRNAs are small non-coding-RNAs that control cell homeostasis and are deregulated in human colorectal cancer (CRC). miR-21 up-regulation is frequent in CRC and represents a driver for tumor initiation and progression. Junctional Adhesion Molecule A (JAM-A) is a tight junction protein controlling para-cellular permeability. JAM-A forms homodimers and activates signaling pathways involved in cell adhesion, polarity and proliferation. For this reason, monoclonal antibodies against JAM-A are currently tested in the preclinical setting as potential targeted therapies. Very little is known about the role of JAM-A in CRC. The aim of our study was to assess whether JAM-A is deregulated in CRC as a consequence of miR-21 over-expression.
Proffered paper session abstracts

Method
JAM-A expression was analyzed by immunohistochemistry in 276 cases of human CRC. MiR-21 and JAM-A expression was analyzed in human CRC cells [RKO, HT29, HCT116, SW620, HCT15, SW480, SW837, SW48, DLD1 (both Wild-Type and Knock-Out for miR-21)] by Real-Time-PCR and Western-Blotting. MiR-21 silencing and over-expression were performed using Locked-Nucleic-Acids and Pre-miR. MiR-21 binding site in JAM-A 3’UTR was predicted using Bioinformatics tools and direct interaction proved by Luciferase assays.

Results
JAM-A down-regulation was observed in cancer compared to normal adjacent tissues. JAM-A was progressively down-regulated in the progression from normal epithelium, dysplasia, intraepithelial and invasive cancer. Poorly differentiated cancers had total loss of JAM-A. 25% of all cancers showed shifted staining from apical to baso-lateral compartment. Silencing and re-expression of miR-21 in CRC cell lines resulted in increase and down-regulation of JAM-A protein expression respectively. Luciferase reporter assay experiments were able to define the potential seed region by which miR-21 interacts with JAM-A 3’UTR.

Conclusion
Our data suggest that JAM-A expression is deregulated by miR-21 and represents a novel miR-21 target. Understanding the mechanisms of JAM-A loss or re-localization may help to stratify patient’s treatment identifying patients who may benefit from anti-JAM-A monoclonal antibodies.

Deep analysis of signalling plasticity in a breast cancer kinase network during acquisition of resistance to PI3K and mTORC1/2 inhibitors
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15.05 – 15.15, Room 3A

Background
Inhibitors against phosphoinositide 3-kinases (PI3K) and mTOR complex 1 and 2 show promise for the treatment of different cancer types. Here, we investigated how kinase signalling circuitry is remodelled when cancer cells become resistant to GDC-0941 and Ku-0063794 (inhibitors having PI3Ks and mTORC1/2, respectively, as their intended targets).

Method
By chronic exposure of MCF7 cells to the inhibitors, we obtained three clones resistant to Ku-0063794 and three resistant to GDC-0941. The phosphoproteomes of these resistant cells were compared to those of parental MCF7 cells using label-free quantitative mass spectrometry.

Results
We quantified >10,000 phosphorylation sites across these resistant clones in two biological and three technical replicates per clone, leading to the acquisition of 410,000 quantitative data points. We identified 805 phosphopeptides that were markers of signalling route activity, and which could be used to quantify the activities of >40 signalling pathways. We observed that mTOR and PI3K signalling remained inhibited in resistant cells, indicating that the compounds were effective in inhibiting their respective target in resistant cells. We found several signalling pathways, having MEK, Erk and PKB/AKT as their members, which were more active in resistant cells relative to the parental line. Interestingly, the patterns of signalling pathway activation were very different in cells resistant to the PI3K inhibitor.
relative to those resistant to the mTOR compound. While we found several phosphorylation sites that were inhibited by both GDC and by Ku, these compounds also inhibited distinct subsets of phosphorylation sites. These data were confirmed by the use of other PI3K and mTOR inhibitors with different chemical structure.

**Conclusion**

Chronic exposure to a PI3K inhibitor remodelled signalling differently compared to inhibiting mTORC1/2. These observations were consistent with the effects of the two inhibitors on the phosphoproteomes of our cell models.

**Acknowledgements**

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**Pan-genomic analysis of hypoxic breast cancer reveals IncRNAs associated with clinicopathological features**

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15.15 – 15.25, Room 3A

**Background**

Transcriptional responses to hypoxia are central to the pathogenesis of many types of cancer. Activated by both oncogenic pathways and tumour hypoxia, these promote an aggressive tumour phenotype leading to poor patient prognosis. To date, pan genomic analyses of these responses have focussed on protein-coding genes. However, it is now recognised that many transcripts have functions that do not include coding for proteins. Here, we comprehensively profile this non-coding transcriptional output in hypoxia.

**Method**

We undertook an integrated pan genomic analysis of normoxic and hypoxic MCF7 breast cancer cells, employing RNA-seq of polyA selected and ribosomally depleted transcripts together with ChiP-seq for the major hypoxia-inducible transcription factor HIF and for chromosomal markers of active transcription (RNApol2 and histone H3K4 methylation). We further assessed these responses following knockdown of HIF transcription factors using RNAi.

**Results**

We establish a computational pipeline of strand specific ribo-depleted RNA-seq data to detect regulated non-coding transcripts including piwiRNA, miRNA, tRNA, sn/snoRNA, and IncRNA. Compared to other classes snRNAs and tRNAs are globally downregulated, whilst a significant number of IncRNAs are upregulated. These upregulated IncRNAs are associated both with chromosomal markers of transcriptional activation and with HIF binding, indicating direct transcriptional activation of non-coding transcripts by HIF. Dependence of IncRNAs on HIF was further confirmed by HIF RNAi. In addition we describe 105 "novel" previously unannotated transcripts bearing chromosomal marks of bon-fide genes. Four hypoxically induced IncRNAs were then analysed in 148 breast tumours and associated with clinicopathological features.

**Conclusion**

Our findings extend knowledge of the hypoxic transcriptional response into the spectrum of non-coding transcripts. We demonstrate that HIF can transcriptionally activate IncRNAs in addition to coding transcripts and link these to
Volatile biomarkers discriminate between bronchial epithelial cells with distinct mutations

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15.25 – 15.35, Room 3A

Background

The genetic basis for lung cancer specific breath detection is supported by the fact that artificial olfactory systems (e.g. NaNose), used to detect volatile organic compounds (VOCs) in headspace samples from cancer cell-lines, can discriminate between cells with different mutations [1]. However, the genome of cancer cell-lines is complex, and often aneuploid, and it is difficult to attribute VOC signatures to specific oncogenic pathways. Therefore in this study we have made use of diploid, immortalised, human bronchial HBEC cell-lines with specific cancer-related mutations [2] in order to investigate whether individual mutations can contribute to significant changes in patterns of VOCs.

Method

HBEC cell-lines carrying the K-RasV12 mutation, knock-down of p53 or both were compared with parental HBEC cells and with each other. Headspace samples were collected by passive sampling with Tenax and measured by either GC-MS or using NaNose sensors. Individual VOCs were compared (GC-MS) and discriminatory patterns (in GC-MS and NanNose data) were identified by Discriminant Factor Analysis (DFA).

Results

In analysis of GC-MS data, 28 VOCs were differentially expressed between at least 2 cell-lines (Wilcoxon pairwise test P<0.05) and DFA analysis identified 4 VOCs that provided discrimination of between 86 and 100% accuracy (with leave-one-out cross-validation). NaNose detection demonstrated that DFA was able to discriminate samples based on their cell-line of origin and accurately predict mutation type.

Conclusion

Taken together our results demonstrate that minimal genetic changes in bronchial airway cells can lead to detectable differences in levels of specific VOCs or sensor output, presumably due to alterations in metabolic output. These data support the possible use of artificial olfactory systems in detection of early forms of lung cancer, or cancers with specific patterns of mutation.

Acknowledgements

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References

CCP Score: A novel genetic test for prostate cancer

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15.35 – 15.45, Room 3A

Background

The natural history of prostate cancer is highly variable and difficult to predict. Improved tools are needed to match treatment to a patient’s risk of progression. We developed an expression signature composed of genes involved in cell cycle progression (Prolaris) and tested its utility in prostate cancer.

Method

We developed an expression signature composed of 31 cell cycle progression and 15 housekeeper genes. An expression score (Prolaris score) was derived as the mean of all cell cycle progression genes. The signature was tested at disease diagnosis in two conservatively managed cohorts (N=337 and 349), after radical prostatectomy in two cohorts from the U.S. (N=366 and 413), and after external beam radiation therapy (N=141). All studies were retrospective.

Results

The CCP signature was a highly significant predictor of outcome in all five studies. In conservatively managed patients, the Prolaris score was the dominant variable for predicting death from prostate cancer in univariate analysis (p = 6.1 x 10-22 after diagnosis by TURP, and p = 8.6 x 10-10 after diagnosis by needle biopsy). In both studies, the Prolaris score remained highly significant in multivariate analysis making it a stronger predictor of disease-specific mortality than other prognostic variables. After prostatectomy, Prolaris predicted biochemical recurrence (BCR) in univariate analysis (S&W p = 5.6 x 10-9; UCSF p = 2.23 x 10-6) and provided additional prognostic information in multivariate analysis (S&W p = 3.3 x10-6; UCSF 9.5 x10-5). After radiation therapy, Prolaris predicted BCR in univariate (p=0.0017) and multivariate analysis (p=0.034). In all five studies the HR per unit change in the Prolaris score was remarkably similar, ranging from 1.89 to 2.92, indicating that the effect size for the Prolaris score is robust to clinical setting and patient composition.

Conclusion

The Prolaris test predicts prostate cancer outcome in multiple patient cohorts and diverse clinical settings. In all cases, it provides information beyond clinicopathologic variables to help differentiate aggressive from indolent disease.

References


Discussion

15.45 – 16.00
The cancer cell and model systems I

Hosted by Caroline Dive, Cancer Research UK Manchester Institute, UK

BACR AstraZeneca Frank Rose Award: The signalling networks regulating cell shape

Chris Bakal
The Institute of Cancer Research, London, UK
14.30 – 14.45, Room 11

Unlike most cells in adult organisms, metastatic cells evolve the ability to change their shape into forms capable of migration and tissue invasion. The shape-shifting ability of metastatic cells is due to the rewiring of the signalling networks that regulate shape in response to the environment. However the precise nature of the shape changes made by metastatic cells, and how the architecture and dynamics of signalling networks are altered in metastatic versus non-metastatic cells is poorly understood. As tumour cell metastasis is the primary cause of death in ~90% of cancer patients, understanding the morphological processes that underpin the metastatic process will provide novel therapeutic opportunities.

The primary goal of my laboratory is to understand the fundamental relationship between cell function, shape, and signal transduction in the context of health and disease. Specifically we: 1) use state-of-the-art RNAi screens and rigorous statistical analyses to describe the signalling networks regulating cell shape, as well as to understand how the biophysics of signalling is influenced by shape; 2) perform in vivo studies to identify genes required for the dynamic shape changes underpinning metastasis; 3) implement large-scale combinatorial RNAi screens to map genetic interactions regulating cell shape; 4) develop mathematical models to describe complex signalling dynamics that leverage single-cell data.

The Hippo pathway polarises the actin cytoskeleton during collective migration of Drosophila border cells

Ichha Khanal, Eliana Lucas, Pedro Gaspar, Georgina Fletcher, Cedric Polesello, Nicolas Tapon, Barry Thompson
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14.45 – 14.55, Room 11

Background
Collective cell migration is essential for morphogenesis, wound healing and immune responses. It also plays an important role during tumour cell invasion.

Method
Using the well-established Drosophila Border Cell (BC) migration model, we use genetic approaches and live imaging to show a novel role for the conserved Hippo (Hpo) pathway in collective cell migration.

Results
The Hpo pathway is known to control tissue growth by regulating cell proliferation and apoptosis, which involves signalling to the nucleus via the transcriptional co-activator Yorkie (Yki). We find that in the context of migration, Hpo and Warts (Wts) – the core kinases of the signalling cascade – act to control the polarisation of the actomyosin cytoskeleton in order to promote directional migration of the BC clusters. Disruption of Hpo signalling in hpo and wts mutants cause severe BC migration delays in 60% of the egg chambers. In addition, we find that the Hpo signalling acts independently of Yki nuclear signalling. We show that the upstream components of the pathway – Expanded, Kibra and Merlin – localise with apical polarity determinants. More importantly, we show that the BC migration delay in wts mutants can be rescued by overexpressing the F-actin Capping proteins (Cp) or by making mutants of their inhibitor – Enabled (Ena).
Conclusion
Thus, we put forward a novel mechanism where cell polarity determinants signal through Hpo and Wts to regulate the activity of Cp and Ena, which then act to polarise the actomyosin cytoskeleton and allow directional movement.

References

NRP1 drives tip-cell selection downstream of Notch signaling by inhibiting ALK5 activation
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14.55 – 15.05, Room 11

Background
Sprouting angiogenesis describes the formation of blood vessels from preexisting ones, a process guided by leading endothelial tip-cells, followed by stalk-cells. The transient specification of both cell fates is mediated by DLL4/NOTCH signalling, primarily actuated by vascular endothelial growth factor (VEGF) and the corresponding receptor, VEGFR-2. The ability of a cell to outcompete its neighbour is determined by VEGFR signalling mediated production of DLL4 and subsequent activation of NOTCH in the adjacent cell. The stalk-cell phenotype, induced by NOTCH, is reinforced by SMAD signalling through a crosstalk between both pathways. However, the downstream effectors of NOTCH and the molecular link to SMAD signalling in tip-cell competition are unknown.

Method
We established a chimeric embryoid body sprouting assays and furthermore use blastocyst injection and analysis of chimeric retinal vessels to investigate the influence of differential protein expression on cell competition and tip/stalk selection.

Results
We identified Neuropilin-1 (NRP1) as a critical NOTCH-regulated determinant of tip/stalk specification. Endothelial cells lacking one or both functional alleles of NRP1 are unable to form tip-cells when competing with wildtype cells. Inhibiting NOTCH is not sufficient to rescue the profound stalk-cell phenotype of NRP1 deficient cells. Thus, we identify NRP1 as the first bona fide downstream effector of NOTCH signalling in regulating angiogenesis. NRP1 was previously described as co-receptor of VEGFR-2, however we find that NRP1 functions independently of VEGFR-2 during tip/stalk selection. Furthermore, our data provides the missing link between NOTCH and SMAD signalling in stalk-cell specification, by revealing NRP1 as negative regulator of the TGF-β/ALK5/SMAD2 pathway. In contrast to NOTCH, inhibition of ALK5 quantitatively restores the ability of NRP1 deficient cells to form tip-cells.

Conclusion
We conclude that differential NRP1 levels act as key effectors downstream of NOTCH by regulating endothelial ALK5/SMAD2 signalling during tip/stalk-cell selection, a novel link that might be important in targeting tumour angiogenesis.
Tetraploidy is permissive for chromosomal instability and accelerates cancer genome evolution

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15.05 – 15.15, Room 11

Background
An increase in ploidy is one of the hallmarks of many different cancer types, despite polyplloid cells being observed rarely in somatic tissues. A complete doubling of the genome, or tetraploidy, has been proposed to be a precursor to aneuploidy (an unbalanced chromosome number) at the onset of carcinogenesis. However tetraploid cells have also been observed at later stages of tumour growth, suggesting polyplloid could also play a role in late emerging tumour phenotypes. We aimed to investigate the effect of polyplloid on long-term genomic stability.

Method
We isolated rare naturally occurring tetraploid cells from the stable diploid colorectal cancer cell line HCT-116. Both diploid and tetraploid clones were grown continuously in culture for over a year, and their genomic instability measured at select time points by methods including clonal FISH, live-cell imaging and SNP6.0 CGH arrays.

Results
Using our isogenic cell line system we observe that tetraploid clones have the ability to tolerate and propagate both numerical and structural chromosome aberrations, whereas the diploid clones remain stable over time. Strikingly all the tetraploid clones show convergent loss of chromosome 4q by later passage numbers. We show that this chromosome region is also lost in highly unstable colorectal tumours, meaning that our system is recapitulating losses seen in vivo.

Conclusion
In a stable diploid cell line, we show that a tetraploidisation event can lead to tolerance of chromosomal instability. We are now investigating how tetraploidy may have conferred this tolerance. Furthermore we see that tetraploidy can accelerate cancer genome evolution, as all tetraploid clones show convergent loss of a chromosome region that is associated with genome instability in vivo. We are interested in whether this chromosome region has a function in the toleration and propagation of chromosomal instability.

Lineage tracing reveals the cellular basis of early metastasis in oesophageal squamous carcinoma

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15.15 – 15.25, Room 11

Background
Oesophageal squamous cell carcinoma has a poor prognosis and is characterised by early invasion and metastasis. Here we apply large scale genetic lineage tracing and statistical physics to resolve cell behaviour in a new model of oesophageal cancer development in transgenic mice.

Method
To generate tumours, we used Sorafenib, a multikinase inhibitor that causes cutaneous squamous cell carcinoma (SCC) as a side effect in cancer patients. Mice carrying a conditional fluorescent protein reporter allele and an inducible form of cre recombinase were treated with a low dose of the cigarette derived carcinogen, diethylnitrosamine (DEN), followed by Sorafenib or vehicle control. Cells were then genetically labelled¹. We applied statistical physics to resolve cell behaviour from the clone size distributions.
Results
Treatment with Sorafenib alone produces dramatic increases in normal oesophageal progenitor cell division and stratification rates, but did not alter the normal balanced production of proliferating and differentiating cells by oesophageal progenitors. In combination with DEN, however, Sorafenib produces multiple tumours, whereas none are seen in DEN + vehicle controls. The lesions appear intraepithelial by conventional histology, but confocal imaging reveals stromal inflammation, associated with Stat3 phosphorylation, angiogenesis and lymphangiogenesis, all features of invasive oesophageal SCC. Lineage tracing within tumours reveals a dramatic change in cell dynamics. The lesions grow through a combination of increased proliferation, generating cells at double the rate of uninvolved epithelium, and a block in cell shedding leading to the accumulation of differentiating cells. Remarkably, genetically labelled keratinocytes are seen undergoing epithelial-mesenchymal transition, invading the stroma and entering blood and lymph vessels.

Conclusion
Lymphovascular intravasation occurs from squamous tumours which are intraepithelial by conventional histology and have marked effects on the underlying stroma usually associated with invasive lesions. These findings explain the early metastasis of oesophageal SCC and validate a new model to test therapeutic interventions.

Acknowledgements
We thank Esther Choolun and the staff of the ARES facility for expert technical assistance.

References

BACR Translational Research Award: Monitoring the cancer genome in plasma using circulating tumour DNA
Nitzan Rosenfeld
Cancer Research UK Cambridge Institute, University of Cambridge, UK
15.25 – 15.40, Room 11

In patients with solid malignancies, cell-free DNA carrying tumour-specific sequences can be found in body fluids such as blood plasma. This circulating tumour DNA (ctDNA) contains representation of the entire cancer genome, broken down into short mutation-carrying fragments, whose relative levels vary in response to treatment and progression. Different approaches to the study of ctDNA can work together to provide a window for noninvasive analysis of the cancer genome and its dynamics. Quantification of ctDNA levels may be useful as a prognostic biomarker and to assess response to treatment. When cancer overcomes treatment and progresses, the fraction of mutant alleles in plasma DNA can reach levels of 10%–20% or more, which makes it possible to study cancer evolution noninvasively by whole-genome or exome analysis of plasma DNA. Sensitivity and resistance to targeted therapies are often associated with known mutations in hotspot loci or genes. In advanced cancer patients, the status of pre-defined mutations can be analysed noninvasively using circulating plasma DNA as a liquid biopsy. Targeted sequencing of limited regions in circulating DNA can allow identification of de novo mutations, even when these are present as rare fragments. This also facilitates parallel quantification of multiple mutations in plasma, which can indicate the relative systemic burden of different mutations or clones. Routine monitoring for sensitizing and resistance-conferring mutations may provide a framework for rational adaptive cancer therapy, providing real-time information on mutation levels to guide treatment against the most aggressive or treatable clones.
Clinical trials

Hosted by Ricky Sharma, Gray Institute for Radiation Oncology & Biology and Oxford University Hospitals NHS Trust, UK

Clinical outcomes in patients with castrate-refractory prostate cancer (CRPC) metastatic to bone randomised in the factorial TRAPEZE trial to docetaxel (D) with strontium-89 (Sr89), zoledronic acid (ZA), neither or both

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14.30 – 14.40, Hall 1A

Background

Bony metastatic CRPC has a poor prognosis and high morbidity. TRAPEZE is a factorial RCT using 3 agents, D, ZA and Sr89. All have palliative benefits and are used in bony metastatic CRPC to control bone symptoms and (for D) to prolong survival. ZA is commonly combined with D in practice but evidence that the combination is effective is lacking and costs considerable. Sr89 is generally used as a palliative therapy in patients unfit for chemotherapy. Phase II analysis confirmed the safety and feasibility of combining these agents.

Method

Patients were randomised to receive 6 cycles of D plus prednisolone: alone, with ZA, with a single dose of Sr89 after cycle 6 or both. Primary outcomes were clinical progression-free survival (CPFS: pain progression, SRE or death) and cost-effectiveness. Secondary outcomes were SRE-free interval (SREFI), total SREs and overall survival (OS). The Log rank test and Cox regression modelling were used to determine clinical effectiveness.

Results

TRAPEZE randomised 757 patients; median age 68.7 yrs; ECOG 0: 40% 1: 52% 2: 8%; prior RT 45%; median PSA 144 (IQR 51, 354). Provisional stratified log rank analysis of CPFS did not reach statistical significance for either agent (Sr89 p=0.11, ZA p=0.45). Cox regression analysis adjusted for all stratification variables showed benefit of Sr89 on CPFS (HR=0.845; 95%CI 0.72, 0.99, p=0.036) and confirmed no effect of ZA (p=0.46). ZA did show a significant effect on SREFI (HR=0.76; 95%CI 0.63, 0.93, p=0.008). There was no effect of either agent on overall survival (Sr89 p=0.74, ZA p=0.91).

Conclusion

Sr89 after 6 cycles of docetaxel improved CPFS but not OS. ZA did not improve CPFS or OS but did significantly improve
median SREFI, mostly post progression suggesting a role as post chemotherapy maintenance therapy. Further health economic and QoL analyses are pending.

A polyphenol rich whole food supplement slows PSA progression in men with prostate cancer: A double-blind, placebo-controlled randomised trial - The NCRN Pomi-T study

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14.40 – 14.50, Hall 1A

\textbf{Background}

Polyphenol rich foods such as pomegranate, green tea, broccoli and turmeric have demonstrated anti-neoplastic effects in cell lines and animal models, including anti-angiogenesis, pro-apoptotic and reduced proliferation. Although some have been investigated in small phase II studies this combination has never been evaluated within an adequately powered RCT.

\textbf{Method}

203 men, aged 53-89 yrs (average 74 yrs), had histologically confirmed prostate cancer, 59% managed with primary active surveillance (AS) and 41% with watchful waiting experiencing a progressive PSA relapse following radical intervention. They were randomised to receive a b.d. oral capsule containing a blend of pomegranate seed, green tea, broccoli and turmeric or an identical placebo for 6 months. Four men withdrew after randomisation.

\textbf{Results}

Of the remaining 199 men, the median rise in PSA in the FSG was 14.7\% (95\% CI 3.4-36.7\%) as opposed to 78.5\% in the PG (95\% CI 48.1-115.5\%). This difference of 63.8\% was significant (p=0.0008) using an analysis of covariance. The number of men with a stable PSA (lower or the same value) at trial completion was 46\% in the FSG as opposed to 14\% in the PG (32\% difference, chi\textsuperscript{2}, p=0.00001). There were no significant differences in PSA\% change within the predetermined subgroup analysis of age, Gleason grade, treatment category or BMI. There were no differences in cholesterol, blood pressure, blood sugar or C-reactive protein between the two groups. 24\% men recorded events in the FSG and 34\% in the PG (non significant). Mild gastro-intestinal effects were most common (17\%) in the FSG but 8\% of these included an improvement in stool quality.

\textbf{Conclusion}

This study found a highly statistically significant short term favourable effect on the percentage rise in PSA in this cohort of men with prostate cancer managed with AS or WW following ingestion of this well tolerated specific blend of concentrated foods (Pomi-T). Future trials will look at the longer term clinical effects and the benefits for men receiving ADT.

\textbf{Acknowledgements}

Gratitude to the charity Prostate Action for partial funding.
The DietCompLyf study: A prospective cohort study of breast cancer survival and phytoestrogen consumption

Ruth Swann1, Annie Perkins1, Louiza Velentzis2, Cristian Ciria3, Susan Dutton3, Angela Mulligan4, Jayne Woodside5, Marie Cantwell5, Anthony Leathem6, Claire Robertson7, Miriam Dwek1

1University of Westminster, London, UK, 2Cancer Council New South Wales, Sydney, Australia, 3University of Oxford, Oxford, UK, 4University of Cambridge, Cambridge, UK, 5Queen’s University Belfast, Belfast, UK, 6University College London, London, UK

14.50 – 15.00, Hall 1A

Background
Breast cancer survival rates vary geographically in part reflecting variations in the diet and lifestyle of different populations. The DietCompLyf study is the largest prospective observational study to date to examine the relationship between diet and lifestyle and breast cancer recurrence and survival rates of patients in the UK.

Method
3,159 women with grade I-III breast cancer were recruited onto the study 9-15 months post-diagnosis. Recruitment took place between 1997 and 2010 from 56 hospitals across the UK. Clinico-pathology, diet, lifestyle, general health and quality of life is documented annually for up to 5 years. Blood and urine samples enable biomarker, nutrigenomic and validation studies. The characteristics of the cohort at recruitment and their reported pre-diagnosis dietary intake of foodstuffs with oestrogen-like properties (phytoestrogens: isoflavones and lignans; from the EPIC-Norfolk food frequency questionnaire) have been assessed.

Results
By descriptor, the majority of patients were post-menopausal (65%), with a grade II (46%), oestrogen receptor positive (82%) tumour, less than 20 mm diameter (50%), and lymph node negative (62%). The median follow-up is 58 months from diagnosis. Return rates for questionnaires at recruitment was at least 85% and almost all patients (≥94%) contributed biological samples. Multivariate analysis has shown isoflavone intakes to be higher in younger patients, non-smokers, those who had breast-fed and taken supplements (p<0.05). Lignan intakes were higher in older patients, ex-smokers, those who had breast-fed, taken supplements, had a lower BMI at diagnosis, lower age at menarche and were nulliparous (p<0.05).

Conclusion
A significant inverse association has emerged between pre-diagnosis phytoestrogen consumption and possession of breast cancer risk factors. The data from DietCompLyf will continue to provide the necessary evidence base on which to test dietary and lifestyle recommendations for breast cancer patients, the overall aim of which is to reduce breast cancer recurrence rates.

Acknowledgements
The DietCompLyf study is funded by Against Breast Cancer (registered charity number 1121258) and supported by the NCRN. We thank all the clinical staff, including nurses and patients for their participation.
Adjuvant Tamoxifen To offer more? (aTTom) - a randomised comparison of continuing adjuvant tamoxifen to 10 years compared to stopping after 5 years among 6953 women with ER positive or ER untested early breast cancer: Overall and subgroup findings

Daniel Rea1, Richard Gray2, Kelly Handley1, Sarah Bowden1, Helena Earl1, Christopher Poole3, Tom Bates2, John Dewar2, Zenon Rayter2, Martin Lee2
1University of Birmingham, Birmingham, UK, 2University of Oxford, Oxford, UK, 3University of Cambridge, Cambridge, UK, 4University of Warwick, Coventry, UK, 5University of Dundee, Dundee, UK, 6University of Bristol NHS Trust, Bristol, UK, 7William Harvey Hospital, Ashford, UK, 8NHS England, Coventry, UK
15.00 – 15.10, Hall 1A

Background
Tamoxifen given for 5 years after surgery for ER-positive early breast cancer reduces recurrence and breast cancer mortality and is more effective than treatment for shorter durations. It has been uncertain what advantage there may be to extending tamoxifen treatment to 10 years.

Method
6953 women with ER+ (n=2755), or ER untested (4198) invasive breast cancer from 176 UK centres, relapse free after 5 years of prior adjuvant tamoxifen, were randomised to stop tamoxifen or continue to year 10. 53% were node negative, 31% node positive and 16% unknown nodal status. Annual follow-up recorded compliance, recurrence, mortality, and hospital admissions.

Results
Median follow up at analysis is 8.6 years Allocation to continue tamoxifen reduced breast cancer recurrence (580/3468 vs 672/3485, p=0.003). This reduction was time dependent: rate ratio (RR) 0.99 during years 5-6 after diagnosis [95%CI 0.86-1.15], 0.84 [0.73-0.95] during years 7-9, and 0.75 [0.66-0.86] later. Longer treatment reduced breast cancer mortality (392 vs 443 deaths after recurrence, p=0.05), RR 1.03 [0.84-1.27] during years 5-9 and 0.77 [0.64-0.92] later; and overall mortality (849 vs 910 deaths, p=0.1), RR 1.05 [0.90-1.22] during years 5-9 and 0.86 [0.75-0.97] later. Non-breast-cancer mortality was little affected (457 vs 467 deaths, RR 0.94 [0.82-1.07]). There were 102 vs 45 endometrial cancers RR=2.20 (1.31-2.34, p<0.0001) with 37 (1.1%) vs 20 (0.6%) deaths (absolute hazard 0.5%, p=0.02). Rate ratios for recurrence from years 2 onwards were not significantly affected by age with RR <55 years 0.70 [0.53-0.92], RR >55 years 0.80 [0.68-0.94] or nodal status: node-negative RR 0.80 [0.64-1.0] node-positive 0.73 [0.58-0.91].

Conclusion
aTTom confirms the recently reported findings of the complementary International ATLAS study that, continuing tamoxifen to year 10 rather than just to year 5 produces further reductions in recurrence and breast cancer deaths. The proportional reduction in recurrence was unaffected by age or nodal status. Benefits from continuing tamoxifen treatment beyond year 5 emerge only after 7 years from start of treatment for recurrence and 10 years for mortality.

Acknowledgements
Funding CR-UK and MRC.

References
PETROC / OV21 Randomised phase II/III Trial of PEritoneal Treatment for Ovarian Cancer: Initial results of the phase II study in preparation for extension to phase III. A collaborative trial of the NCRI, NCIC, GEICO, and SWOG Gynaecological Cancer Study Groups

Chris Gallagher¹, Alice Clark², Mandy Feeney³, Lindsay James⁴, Charles Gourley⁵, Marcia Hall⁶, Geoff Hall⁷, Jonathan Ledermann³, ²

¹St Bartholomew’s Hospital, London, UK, ²University College Hospital, London, UK, ³Cancer Research UK and UCL Cancer Trials Centre, London, UK, ⁴Western General Hospital, Edinburgh, UK, ⁵Mount Vernon Cancer Centre, Middlesex, UK, ⁶St James’s Hospital, Leeds, UK

15.10 – 15.20, Hall 1A

Background
A meta analysis of phase III trials of post operative intraperitoneal (IP) chemotherapy in epithelial ovarian cancer, fallopian tube and primary peritoneal cancer in 853 patients with 6 years followup (GOG 114 and 172) has shown a reduction of 16% in risk of progression, 17% in risk of death, and increased median progression free (20 to 25 months), and overall (51 to 62 months) survival. PETROC/OV21 is designed to investigate women not able to be optimally debulked at primary surgery who have had primary IV chemotherapy and optimal interval debulking followed by IV or IP treatment, with dose paclitaxel plus carboplatin or cisplatin.

Method
Patients with advanced stage III or IV (pleural effusion) disease for whom optimal primary debulking surgery was not possible because of bulk of disease or comorbidity received three cycles of IV carboplatin and paclitaxel and interval debulking surgery. 150 patients with residual disease <1cm entered a randomised phase II three arm study of three more cycles of chemotherapy followed by three monthly CT scan and CA125 until progression. The treatment arms were: standard IV paclitaxel and carboplatin, or experimental IP plus IV paclitaxel and either IP carboplatin, or IP cisplatin. The endpoints were recruitment rate, completion of treatment and toxicity, and 9 month progression rate to select the preferred experimental arm for a phase III study.

Results
150 patients were recruited in 38 centres from February 2010 in Canada, February 2011 in UK and Spain, December 2012 in USA up to February 2013. With 171 now entered 81% had disease too extensive to be optimally debulked at primary surgery, 60% had microscopic only residual disease after interval debulking surgery. 79% completed planned treatment, 9% came off trial with catheter complications, 5% with adverse events, 7% other. There are the expected non-significant toxicity differences between arms, abdominal pain was uncommon and mild.

Conclusion
Intraperitoneal chemotherapy after interval debulking surgery is feasible and safe, recruitment continues while expansion of the number of centres for the two arm phase III study is planned.

Acknowledgements
Study funded by grants from CRUK and NCICanada.
A randomised trial of 72 hour infusional bleomycin in BEP (cisplatin, etoposide and bleomycin) versus conventional weekly bleomycin in patients with metastatic IGCCCG good prognosis disease

Jonathan Shamash1, Robert Huddart2, Stephen Harland3, Johnathan Joffe4, Danish Mazhar5, Alison Birtle6, Jeff White7, Shah Jalal Sarker1, Peter Wilson1, Marita Marshall1, Sarah Vinnicombe8

1 Barts Cancer Institute, London, UK, 2 Royal Marsden Hospital, London, UK, 3 University College London Cancer Institute, London, UK, 4 Institute of Oncology, Leeds, UK, 5 Addenbrooke’s Hospital, Cambridge, UK, 6 Royal Preston Hospital, Preston, UK, 7 Beatson West of Scotland Cancer Centre, Glasgow, UK, 8 Division of Cancer Research, Dundee, UK

15.20 – 15.30, Hall 1A

Background
Bleomycin is an integral part of combination chemotherapy in germ cell tumours. Pulmonary symptoms often dictate drug cessation and death occurs in 1-2% of patients. Circumstantial evidence suggests that continuous infusion may be less toxic.

Method
We conducted a randomised phase 3 study to see whether infusional bleomycin was associated with less pulmonary toxicity. Patients were stratified for smoking, renal dysfunction and age and were randomized to receive either conventional BEP with weekly bleomycin (30000 units /week iv over 30min) or the same doses but administered as a 90000 unit infusion on day 1 over 72 hours. The primary endpoint was CT proven lung toxicity, secondary endpoints included PFS and changes in lung function testing. CT scans and lung function testing were conducted after 1 cycle, end of treatment and 1 year post treatment. Sample size of 210 was calculated to detect a difference of 16% Bleomycin damage with 80% power at the 5% level of significance using 2-sided test.

Results
The median follow-up was 2.5 years. At day 21 of the treatment, 52% patients in the infusional arm had grade 1 or above toxicity compared to 55% in the conventional. At the end of treatment the results were 84% vs 60% and at one year it was 65% vs. 59%. Repeated measures mixed effects model shows no significant difference in percentage of grade 1 and above toxicity between the two arms (Difference=1.63, P=0.09, 95% CI: -0.28, 3.54). However, there was a significantly higher level of grade 2 and above toxicity in patients in the infusion arm (difference=0.8; 95% CI 0.11 to 1.49). Toxicity level was the highest at the end of treatment and in older patients (Age>30). Lung function testing between the two arms failed to show any differences. Two-years PFS rate was 93% in both arms (hazard ratio infusion vs conventional was 0.91; 95% CI 0.33 to 2.52). There was an association between toxicity after 1 cycle and subsequent toxicity at end of treatment and at 1 year (p=0.003).

Conclusion
Infusional bleomycin does not have any advantage over standard administration of bleomycin. Age of patient was the most important predictor of subsequent lung toxicity. Pre treatment lung function did not predict subsequent toxicity. There was an association between lung toxicity after one cycle which may allow patients at risk of subsequent toxicity to be identified early.

Acknowledgements
Cancer Research UK Orchid Cancer Appeal.
Identification of plasma metabolite changes following phosphatidylinositol-3-kinase (PI3K) inhibition with GDC-0941, a potent and selective pan-Class I inhibitor of PI3K: preclinical discovery followed by clinical qualification in a Phase I clinical trial.

Joo Ern Ang1,2, Rupinder Pandher1, Yasmin Asad1, Alan Henley1, Melanie Valent1, Gary Box1, Alexis de haven Brandon1, Richard Baird1, Lori Friedman1, Mika Derynck1, Suzanne Eccles1, Stan Kaye1,2, Paul Workman1, Johann de Bono1,2, Florence Raynaud1,2

1Cancer Research UK Cancer Therapeutics Unit, The Institute of Cancer Research, Sutton, Surrey, UK, 2Drug Development Unit, The Royal Marsden NHS Foundation Trust, Sutton, Surrey, UK, 3Genentech Inc, South San Francisco, California, USA

15.30 – 15.40, Hall 1A

Background
Phosphatidylinositol-3-kinase (PI3K) plays a key role in cellular metabolism. A mass spectrometry-based metabolomic platform was used to identify novel pharmacodynamic plasma metabolite biomarkers of systemic modulation of PI3K signalling.

Method
The preclinical screen included comparisons of tumour-bearing PTEN knockout (+/-) mice with their respective non-tumor-bearing wildtype littermates and athymic mice with or without PTEN/-/- human tumor xenografts. The effect of GDC-0941-treatment versus vehicle was evaluated in xenograft-bearing mice and candidate biomarkers then measured in plasma samples of patients with advanced solid tumours treated in a Phase I clinical trial of GDC-0941.

Results
Thirty plasma metabolites including branched chain and aromatic amino acids, acylcarnitines and phospholipids were down-regulated in the PTEN null models and up-regulated following pharmacologic inhibition using GDC-0941. In patients treated with GDC-0941 (n=41, median age 54 years [range 37-72], 18 males and 23 females, median body mass index 26.4 kg/m² (SD 4.2)), time- and dose-dependent changes in 26 candidate metabolites were observed post-dose on day 1; the magnitudes of treatment-associated changes were greater than baseline variability. All these changes were consistent with the tumor-bearing mouse models apart from the long chain acylcarnitines where a significant decrease was observed in-keeping with changes in the non-tumor-bearing mice. All observed changes resolved after a 1-week drug washout and were recapitulated on day 15 after a week of continuous oral dosing.

Conclusion
This study provides the first link between systemic modulation of the PI3K pathway and changes in plasma metabolites which may have utility as minimally invasive pharmacodynamic biomarkers. These findings provide additional support for the association of insulin resistance with branched-chain amino acids and related metabolites following PI3K inhibition.

Tumour- and treatment-related colostomy rates following 5Fluorouracil (5FU) and Mitomycin (MMC) or 5FU and Cisplatin (Cisp) chemoradiation (CRT) with or without maintenance chemotherapy in squamous cell carcinoma of the anus: Results of the randomised phase III trial ACT II

Rob Glynne-Jones1, Latha Kadalayil2, Helen Meadows2, David Cunningham3, Les Samuel4, Ian Geh5, Charles Lowdell6, Roger James7, Sandy Beare1, Rubina Begum2, Jonathan Ledermann1, David Sebag-Montefiore6

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James’s Institute of Oncology, Leeds, UK
15.40 – 15.50, Hall 1A

**Background**
In the ACT II trial, chemoradiation with 5FU/CisP had similar CR and overall toxicity to 5FU/MMC. Maintenance chemotherapy did not improve PFS. We aimed to determine tumour/treatment-related colostomy rates following CRT and maintenance chemotherapy in squamous-cell carcinoma of the anus.

**Method**
The ACT II trial recruited 940 patients and compared CRT using cisplatin (CisP)/ 5-Fluorouracil (5FU) (n=468) with mitomycin (MMC)/5FU (n=472) and maintenance chemotherapy (n=448) with no maintenance (n=446). We investigated the association between colostomy-free survival (CFS) and progression-free survival (PFS) with age, gender, T-stage, N-stage, treatment and baseline haemoglobin.

**Results**
Median follow-up was 5.1 years (n=884 evaluable/940); tumour site canal (84%), margin (14%); stage T1/T2 (52%), T3/T4 (46%); N+(32%), N0 (62%). 20/118 (17%) colostomies fashioned prior to CRT were reversed within 8 months. 112 patients had a post-treatment colostomy due to persistent disease (98) or morbidity (14). 52% (61/118) of all pre-treatment colostomies were never reversed. The 5-year CFS rates were 68% MMC/Maint, 70% CisP/Maint, 68% MMC/No-maint and 65% CisP/No-maint. CRT with CisP did not improve CFS when compared to MMC (HR: 1.04, 95% confidence interval: 0.82-1.31, p=0.74). The 5-year CFS rates were higher for T1/T2 (79%) than T3/T4 (54%) tumours and higher for node-negative (72%) than node-positive (60%) patients. Significant predictors of CFS were gender, T-stage and haemoglobin. Treatment factors had no impact on outcome. Similar associations were found between PFS and tumour/treatment-related factors.

**Conclusion**
We achieved good CFS in a multicentre setting, but neither CRT with 5FU/CisP nor maintenance chemotherapy improved CFS over the standard of 5FU/MMC CRT. In total 34% (61/177) of all colostomies were baseline fashioned prior to treatment and never reversed. The low risk of colostomy for late effects (1.7%) is likely to be associated with the modest total radiotherapy dose. The predictive factors for CFS were T-stage, gender and baseline haemoglobin.

**Acknowledgements**
All participating UK Institutions and patients. ISRCTN number: 26715889, NCRI, Cancer Research UK grant number C444/A620.

**Discussion**
15.50 – 16.00

**Treatment decision making, screening and palliative care**

Hosted by Jane Seymour, University of Nottingham, UK
Modafinil for fatigue in lung cancer: multicentre, randomised, double-blinded, placebo-controlled trial: effect, dose response and patient satisfaction

Bee Wee1,4, Susan Dutton1, Kate Fife2, Fiona Blackhall3, Ronja Bahadori4, Rose Wharton1, Mary O’Brien5, Paddy Stone6, Tim Benepe6, Anna Spathis2

1University of Oxford, Oxford, UK, 2Addenbrookes Hospital, Cambridge, UK, 3Christie Hospital, Manchester, UK, 4Oxford University Hospitals NHS Trust, Oxford, UK, 5Royal Marsden Hospital, London, UK, 6St George’s Hospital, London, UK

14.30 – 14.40, Hall 1B

Background

Fatigue is a common, highly disabling symptom in cancer. Modafinil is a novel central nervous system stimulant, which, along with methylphenidate, is cautiously recommended by the 2013 National Comprehensive Cancer Network Guidelines for fatigue. In this Phase IV trial, we assessed the efficacy of modafinil for managing fatigue in lung cancer.

Method

Adults with locally advanced or metastatic non small cell lung cancer (stages III and IV), ECOG performance status (PS) 0-2 and suffering from fatigue (score 5/10 or greater) were randomised 1:1 to modafinil or matched placebo, 100mg daily for 14 days and 200mg daily for a further 14 days. The primary outcome measure was change in the Functional Assessment of Chronic Illness Therapy fatigue subscale (FACIT-fatigue) at 28 days. The trial was powered to detect a 5-point difference with 80% power and 5% significance allowing for 25% attrition. Daytime sleepiness, anxiety and depression, quality of life, safety, dose-response and patient satisfaction were also evaluated.

Results

208 patients were recruited from 24 UK centres. Baseline characteristics were well-balanced. 160 patients completed both baseline and 28 day questionnaires and were included in the modified-ITT analysis. FACIT-fatigue mean change from baseline was modafinil=5.28, placebo=5.11, difference=0.17, (95%CI -4.17, 3.82). Adjustment for baseline fatigue and PS had no impact on outcome. Adverse events were equal. No dose response was seen; the majority of improvement on all scales was seen at 14 days and sustained to 28 days. 47% of the modafinil group and 23% of the placebo group stated the study treatment was not helpful (p=0.132).

Conclusion

Both modafinil and placebo led to a clinically significant 5-point improvement in FACIT-fatigue score, but there was no significant difference between the two groups. This large, well-powered study suggests that there is a large placebo effect and NCCN guidelines should be reviewed.

Acknowledgements

Funders: NCRI Supportive and Palliative Care Lung Cancer award; Sobell House Hospice Charity. With thanks to Lois Sims for her work on data.

Results from the UNBIASED study (UK - Netherlands - Belgium International SEDation study): reported practices of physicians and nurses in three European countries

Jane Seymour1, Luc Deliens2, Judith Rietjens2,3, Sigrid Sterckx4, Jayne Brown5, Agnes van der Heide6

1University of Nottingham, Nottingham, UK, 2Vrije Universiteit, Brussels, Belgium, 3Erasmus MC, Rotterdam, The Netherlands, 4Ghent University, Ghent, Belgium, 5De Montfort University, Leicester, UK

14.40 – 14.50, Hall 1B

Background

Results from the UNBIASED study (UK - Netherlands - Belgium International SEDation study): reported practices of physicians and nurses in three European countries

Jane Seymour1, Luc Deliens2, Judith Rietjens2,3, Sigrid Sterckx4, Jayne Brown5, Agnes van der Heide6

1University of Nottingham, Nottingham, UK, 2Vrije Universiteit, Brussels, Belgium, 3Erasmus MC, Rotterdam, The Netherlands, 4Ghent University, Ghent, Belgium, 5De Montfort University, Leicester, UK

14.40 – 14.50, Hall 1B

Background
Continuous sedation in end of life care is an important and frequently necessary but highly contested intervention in the care of dying patients with otherwise refractory distress. There have been few studies which allow international comparisons to be made and which investigate the perspectives of physicians and nurses from different care settings. The aim of this study was to: examine health care professionals’ experiences of using continuous sedation in end-of-life care for cancer patients and to identify and explain differences in reported practice between UK, Belgian and Dutch practitioners.

Method
Design: Qualitative case study design, based on face to face interviews.
Setting: Hospitals, the domestic home, and hospices or palliative care units attached to hospitals in the UK, Belgium and the Netherlands.
Participants: 57 Physicians and 73 nurses who were involved in the use of continuous sedation until death for 84 cancer patients.

Results
UK respondents reported a continuum of practice from the provision of low doses of sedatives to control terminal restlessness to rarely encountered deep sedation. In contrast, Belgian respondents predominantly described the use of deep sedation, emphasizing the importance of responding to the patient’s request for relief of suffering. Dutch respondents placed emphasis on the making of an official medical decision informed by the patient’s wish where this was known and establishing that a refractory symptom was present before commencing sedation. Respondents employed rationales that showed different stances and values towards four key issues: the preservation of consciousness during dying, concerns about the potential hastening of death, whether they perceived continuous sedation until death as an ‘alternative’ to euthanasia, and lastly, whether they sought to follow guidelines or frameworks for practice. UK nurses were demonstrated to have particular responsibilities for activating ‘anticipatory prescriptions’ in the context of the Liverpool Care Pathway for the Dying Patient.

Conclusion
This qualitative analysis suggests that there is systematic variation in end-of-life care sedation practice and its conceptualization in the UK, Belgium and the Netherlands. Educational programmes tailored at recognizing that practice is situated in and affected by different values and legal contexts may helpfully inform what are otherwise frequently difficult and contentious discussions about practice and policy in sedation.

Acknowledgements
Presented on behalf of the UNBIASED consortium study (UK - Netherlands - Belgium International SEDaration study.

An all-Ireland population-based study of past and current physical and psychological side-effects following prostate cancer treatments
Heather Kinnear¹, Frances Drummond², Linda Sharp², Anna Gavin¹, Lesley Anderson¹
¹Queen’s University Belfast, Belfast, UK, ²National Cancer Registry Ireland, Cork, Ireland
14.50 – 15.00, Hall 1B

Background
In Ireland, prostate cancer is the most common male cancer. Recommendations that men be involved in treatment decision-making require good information on treatment side-effects. Population-based data on side-effects is limited.
This all-Ireland, population-based study investigated physical and psychological side-effects of prostate cancer treatments up to 15 years post-diagnosis.

**Method**

7,000 men diagnosed with primary, invasive, prostate cancer (C61) 1-15 years ago, identified through cancer registries in Northern Ireland (NI) and Republic of Ireland (ROI), received a postal questionnaire (encompassing specific questions on treatments received and side-effects experienced) during 2012.

**Results**

Prostatectomy was more common in ROI, hormone and radiotherapy were more common in NI. Numbers of prostatectomies rose in ROI while other treatments decreased. Urinary symptoms (including haematuria and pain) were common before treatment (36%); urinary incontinence after treatment was also common for 30% of prostatectomy patients and 14% of radiotherapy and hormone therapy patients. Approximately 1 in 6 men experienced impotence before treatment, quadrupling post treatment to 4 in 6 men. Two thirds reported loss of sexual desire post treatment. One fifth reported ongoing bowel problems. One quarter reported depression after treatment, an increase from 1 in 20 before treatment. Sweats/hot flushes and changes in breast tissue were more common with hormone therapy. Men were also asked about regret at having chosen a particular treatment. There was an overall regret score of 12.6%, with prostatectomy patients and those receiving active surveillance/watchful waiting both showing higher levels of regret than other treatment types. Patients reporting incontinence had the highest levels of regret.

**Reduction in interval cancer rates following the introduction of two-view mammography in the UK breast screening programme**

**Amanda Dibden**¹, Judith Offman¹, Dharmishta Parmar¹, Jacquie Jenkins², Jo Slater³, Kathie Binysh⁴, Joan McSorley⁵, Suzanne Scorfield⁶, Pam Cumming⁷, Xiao-Hui Liao⁸, Michael Ryan⁹, Diane Harker¹⁰, Guy Stevens¹¹, Nicola Rogers¹², Roger Blanks¹³, Sarah Sellars¹⁴, Julietta Patrick¹⁵, Stephen Duffy¹


**Background**

The introduction of two-view mammography at incident (subsequent) screens in the National Health Service Breast Screening Programme (NHSBSP) has led to an increased number of cancers detected at screen. However, the effect of two-view mammography on interval cancer rates has yet to be assessed.

**Method**

Routine screening and interval cancer data were collated from all screening programmes in the UK for women aged 50-64, screened between 1 April 2003 and 31 March 2005. Interval cancer rates were compared based upon whether two-view mammography was in use at the last routine screen.
Results
The reduction in interval cancers following screening using two-view mammography compared to one view was 0.68 per 1,000 women screened. Overall, this suggests the introduction of two-view mammography at incident screen was accompanied by a 15-20% reduction in interval cancer rates in the NHSBSP.

Conclusion
The reduction in interval cancers is consistent with the increase in screen detected cancers seen following the introduction of two-view mammography at incident screens. The results provide further evidence of the benefit of the use of two-view mammography at incident screens.

Clinical implications of a prostate cancer risk SNP profile in 2 treatment cohorts
Chee Goh1, Edward Saunders1, Daniel Leongamornlert1, Tokhir Dadaev1, Malgorzata Tymrakiewicz1, Karen Thomas1, Elizabeth Selvadurai2, Ruth Woode-Amisah2, Nadiya Mahmud1, Elena Castro3, David Olmos4, Michelle Guy1, Koveela Govindasami1, Rosemary Wilkinson1, Emma Sawyer1, Ali Amin Al Olama5, Douglas Easton5, Zsofia Kote-Jarai1, Chris Parker1,2, Rosalind Eeles1,2

1The Institute of Cancer Research, London, UK, 2The Royal Marsden NHS Foundation Trust, London, UK, 3Spanish National Cancer Research Centre (CNIO), Madrid, Spain, 4University of Cambridge, UK
15.10 – 15.20, Hall 1B

Background
Genome-wide association studies (GWAS) have identified 77 single nucleotide polymorphisms (SNPs) associated with prostate cancer (PCa) risk. Currently their clinical utility remains undefined. We explore the prognostic role of these SNPs in 2 PCa treatment cohorts.

Method
DNA from patients undergoing active surveillance (AS) or androgen deprivation therapy (ADT) at the Royal Marsden Hospital was analysed. Risk SNPs were genotyped using Sequenom or Fluidigm platforms. The cumulative SNP risk scores for each patient were calculated by summing risk alleles for each of the loci using the weighted effect as estimated in previous studies (log-additive model). For the AS group, the risk scores were analysed against biopsy upgrade and time-to-treatment, to determine their prognostic value. For the ADT group, the risk scores were assessed against time-to-relapse, defined by either biochemical relapse or progression on repeat imaging.

Results
For the AS analyses, 391 patients’ DNA was studied; 31% of those have since undergone treatment and 30% have histological upgrade on repeat biopsies. On univariate analysis, no significant relationship was found when risk scores were analysed against biopsy upgrade or time-to-treatment (p>0.05). There were also no significant differences in outcomes between men in the highest and lowest 25% of the genetic risk distribution.

For the ADT analyses, 567 patients’ DNA was studied. The mean duration of response was 30 months. No significant associations were found when risk scores were analysed as a continuous variable against time-to-relapse, or when analysing differences between the highest and lowest 25% of the risk distribution.
Proffered paper session abstracts

Conclusion
PCa SNP risk scores have not been shown to be prognostic factors in either AS or ADT and so may be more useful for population risk stratification for screening. To our knowledge, this is the first study looking at the potential prognostic significance of the latest GWAS risk SNPs in PCa treatment cohorts.

Over or under treatment? A systematic review and meta-analysis of factors determining change of management in active surveillance for localised prostate cancer
Andrew Simpkin1, Kate Tilling1, Richard M Martin1,2, J Athene Lane1, Freddie C Hamdy3, Lars Holmberg4, David E Neal5, Chris Metcalfe1, Jenny L Donovan1

1School of Social and Community Medicine, University of Bristol, Bristol, UK, 2MRC Centre for Causal Analysis in Translational Epidemiology, University of Bristol, Bristol, UK, 3Nuffield Department of Surgical Sciences, University of Oxford, UK, 4Guy’s Hospital, London, UK, 5Oncology Centre, Addenbrooke’s Hospital, Cambridge, UK
15.20 – 15.30, Hall 1B

Background
Increasingly, men with localised prostate cancer are being monitored as part of active surveillance (AS) programs, but little is known about reasons for stopping AS and receiving radical treatment.

Method
A systematic review with meta-analysis and meta-regression was conducted to estimate the rate, and identify predictors of management change from AS.

Results
22 AS cohorts were eligible (n = 7,111 men) with a median follow-up of 3.7 years (range 1.5 - 7.5 years). Protocols for triggering management change varied considerably between studies. Higher baseline PSA value (pooled hazard ratio (PHR) 1.03, 95% CI 1.01,1.06), Gleason grade > 3+3 (PHR 1.98,95% CI 1.54,2.55) and T-stage ≥ 2a (PHR 1.39,95% CI 1.15,1.70) were associated with higher rate of radical treatment. The management change rate was 84 per 1,000 person years (95% CI 61,106), with heterogeneity between cohorts in this rate (I^2= 96%; p<0.0005). Studies with a scheduled re-biopsy had 50 more men changing per 1,000 person years than other cohorts (95% CI 7,94). Cohorts including men with a Gleason grade above 3+3 had 50 fewer men changing per 1,000 person years (95% CI 9,88). Eight men died of prostate cancer and five developed metastases.

Conclusion
It is unlikely that 84 men per 1000 person years are truly progressing in these early stages cohorts. Some apparent upgrading is inevitable in cohorts with scheduled re-biopsy, due to the detection of higher grade tumour which was missed by chance at first biopsy. Those cohorts admitting men with higher grade tumours saw fewer men overall switching to radical treatment, and this is likely due to a greater requirement for evidence of progression prior to treatment review. Criteria for clinical review should not be triggered by random variation in PSA level and the tumour grades observed, to avoid unnecessarily alarming men, and the prompting of unnecessary radical treatment.

Acknowledgements
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Obesity and the outcome of young breast cancer patients in the UK: The POSH study
Ellen Copson1, Ramsey Cutress1, Bryony Eccles1, Clarice Wong1, Tom Maishman1, Sue Gerty1, Louise Dent1, Douglas Altman2, Lorraine Durcan1, Peter Simmonds1
1Cancer Sciences Academic Unit and Clinical Trials Unit, Faculty of Medicine, University of Southampton, Southampton, UK, 2Centre for Statistics in Medicine, Oxford, Oxford, UK
15.30 – 15.40, Hall 1B

Background
Obese patients with early breast cancer have a poorer prognosis than non-obese patients. Host factors, tumour pathology and treatment issues have been suggested as possible factors. We examined data from the multi-centre Prospective Outcomes of Sporadic and Hereditary breast cancer study to investigate this in pre-menopausal women.

Method
2956 patients aged \( \leq 40 \) at breast cancer diagnosis were recruited from 126 UK hospitals between 2001 and 2007. Details of body mass index (BMI), tumour pathology and treatment were collected. Follow-up data were collected at 6 months, 12 months and then annually. Adjuvant chemotherapy prescriptions were reviewed for 85 patients treated locally.

Results
BMI data were available for 2842 (96.1%) patients: 36 (1.3%) were underweight (BMI<18.5), 1489 (52.4%) were healthy weight (18.5\( \leq \)BMI<25), 784 (27.6%) were overweight (25\( \leq \)BMI<30) and 533 (18.8%) were obese (BMI\( \geq \)30). There was a significant difference in 8-year overall survival between BMI categories (p<0.001), with survival of obese patients (58.6%) almost 15% lower than healthy weight patients (73.3%). Median tumour size was significantly higher in obese patients than normal weight patients (26mm vs. 20mm, p<0.001). Obese patients had significantly more grade 3 tumours (63.9% vs. 58.8%, p=0.042) and node positive tumours (54.6% vs. 49.4%, p=0.040) than normal weight patients. ER negative tumours were more frequent in obese patients than normal weight patients (68.0% vs. 59.9%, p=0.001) whereas the incidence of HER 2 positive tumours was similar (28.2% vs. 27.3%, p=NS). Obese patients were significantly more likely to experience a chemotherapy dose delay than healthy weight patients (33.3% vs. 5.9%, p=0.007).

Conclusion
Obesity at diagnosis is associated with inferior survival in young breast cancer patients. Our data confirms that obesity is associated with biologically adverse tumours. Furthermore, more obese patients receive sub-optimal chemotherapy than healthy weight patients. Further studies will explore the effect of body composition on chemotherapy tolerance.
Parallel sessions

KEY TO THEMES:

D  Diagnosis and therapy
E  Epidemiology and prevention
I  Information, patients and the public
S  Survivorship and end-of-life care
C  The cancer cell and model systems
T  Tumour-specific research

IS  Life-altering late effects and their management in survivors of childhood malignancy
  Hall 1C  Hosted by Rod Skinner, Great North Children’s Hospital and Royal Victoria Infirmary, Newcastle upon Tyne, UK
  16.20 – 16.25  Introduction by the host
  16.25 – 16.50  Frequency, timing and causes of late mortality in survivors of childhood malignancy
      Raoul Reulen, University of Birmingham, UK
  16.50 – 17.15  Female fertility in survivors of childhood malignancy
      Hamish Wallace, University of Edinburgh, Royal Hospital for Sick Children, UK
  17.15 – 17.40  Late effects of childhood cancer: What are the consequences for long-term survivors and how can they be reduced?
      Melissa M Hudson, St. Jude Children’s Research Hospital, Memphis, USA
  17.40 – 17.50  Discussion

T  Molecular stratification and clinical management of adult high-grade glioma
  Hall 1B  Hosted by Colin Watts, University of Cambridge, UK
  16.20 – 16.25  Introduction by the host
  16.25 – 16.50  Predictive markers for response to adjuvant procarbazine, lomustine (CCNU) and vincristine (PCV) in anaplastic oligodendrogliomas and oligoastrocytomas
      Pim French, Erasmus University Medical Centre, Rotterdam, The Netherlands
  16.50 – 17.15  Molecular stratification and clinical management of adult high-grade glioma: Lessons from the elderly trials
      Michael Weller, University Hospital Zurich, Switzerland
  17.15 – 17.40  Intra-tumour heterogeneity reflects cancer evolutionary dynamics: Implications for patient stratification
      Colin Watts, University of Cambridge, UK
  17.40 – 17.50  Discussion
**Parallel sessions**

**E** 'Real world’ data: Opportunities and challenges

Room 11

Hosted by **David Ford**, Swansea University, UK

16.20 – 16.25

Introduction by the host

16.25 – 16.50

Impact of ‘real world data’ on cancer patient outcomes and care

**Anna Gavin**, Northern Ireland Cancer Registry, Queen’s University Belfast, UK

16.50 – 17.15

Title TBC

**Eva Morris**, St. James’ University Hospital, Leeds, UK

17.15 – 17.40

Title TBC

**Tim Hubbard**, Wellcome Trust Sanger Institute, Cambridge, UK

17.40 – 17.50

Discussion

**T** Re-shaping clinical practice in neuroendocrine tumours (NETs)

Room 3A

Hosted by **John Primrose**, University of Southampton, UK and **Juan Valle**, The Christie NHS Foundation Trust, Manchester, UK

16.20 – 16.25

Introduction by the hosts

16.25 – 16.50

Integrated genomic analysis and application of single cell and circulating free DNA sequencing in NET management

**Chrissie Thirlwell**, University College London Cancer Institute and Royal Free Hospital NET Unit, London, UK

16.50 – 17.15

Theranostics: From molecular imaging using PET/CT to personalised therapy of over 1100 patients with neuroendocrine tumours (NETs)

**Harshad Kulkarni**, ENETs Center of Excellence, Zentralklinik Bad Berka, Germany

17.15 – 17.40

Systemic therapy options for NETs: When and what

**Ramón Salazar**, Institut Català d’Oncologia, L’Hospitalet de Llobregat, Barcelona, Spain

17.40 – 17.50

Discussion

**D** Smarter surgery for better cancer outcomes

Room 3B

Hosted by **Dion Morton**, University of Birmingham, UK

16.20 – 16.25

Introduction by the host

16.25 – 16.50

Smarter surgery for better cancer outcomes: Leading the way with breast cancer

**Alastair M Thompson**, Dundee Cancer Centre, UK

16.50 – 17.15

Surgeons and oncologists: Optimising surgery within multimodality treatment

**David Sebag-Montefiore**, University of Leeds, UK and **Simon Bach**, Queen Elizabeth Hospital, Birmingham, UK

17.15 – 17.40

Smarter trial designs in surgical oncology

**Jane Blazeby**, University of Bristol, UK

17.40 – 17.50

Discussion
Parallel sessions

**D** Targeting the epigenome

**Hall 1A** Hosted by Robert Brown, Imperial College London, UK

16.20 – 16.25 **Introduction by the host**

16.25 – 16.50 **Working together to exploit a rich seam of novel epigenetic targets for cancer**

Chas Bountra, University of Oxford, UK

16.50 – 17.15 **Cancer epigenetics: From mechanism to therapy**

Mark Dawson, Cambridge Institute for Medical Research & Wellcome Trust and Cancer Research UK Gurdon Institute, University of Cambridge, UK

17.15 – 17.40 **Targeting EZH2 in haematological malignancies**

Patrick Trojer, Constellation Pharmaceuticals, Cambridge, USA

17.40 – 17.50 **Discussion**

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**IS** The issues with tissues

**Room 4** Hosted by Mairead MacKenzie, Independent Cancer Patients’ Voice, UK

16.20 – 16.25 **Introduction by the host**

16.25 – 16.45 **The critical need for longitudinal tissue and blood sample collection in cancer research**

Mariam Jamal-Hanjani, University College London, UK and Matthew Krebs, Cancer Research UK Manchester Institute, UK

16.45 – 17.05 **Challenges in using samples for clinical research: A pan-European perspective**

Jacqueline Hall, Formerly Head of Translational Research Unit, European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium

17.05 – 17.25 **Consent: Asking the question?**

Hilary Stobart¹ and Helen Bulbeck², ¹Member of PPI Advisory Group and volunteer, Nottingham Health Science Biobank, Nottingham University Hospitals NHS Trust, UK; ²Braintrust, UK

17.25 – 17.50 **Discussion**

Chaired by Bridget Wilkins, Guy’s and St Thomas’s Hospital, London. UK
Life-altering late effects and their management in survivors of childhood malignancy

Introduction
Rod Skinner
Great North Children’s Hospital and Royal Victoria Infirmary, Newcastle upon Tyne, UK
16.20 – 16.25, Hall 1C

The aim of this session is to describe some of the most severe and/or life-changing toxicities that may occur in survivors of childhood malignancy. It will include:

- Epidemiological research that has informed efforts to improve care of survivors and reduce frequency of late mortality.
- Laboratory and clinical research/technological advances to improve the management of fertility impairment in female survivors.
- An overview of survivorship issues in general, with particular emphasis on how survivors lives are changed.

Frequency, timing and causes of late mortality in survivors of childhood malignancy
Raoul Reulen
University of Birmingham, UK
16.25 – 16.50, Hall 1C

Due to marked advances in curative therapy for childhood cancer – mainly the introduction of modern chemotherapy in the 1960s – the five-year survival rate after childhood cancer has substantially improved over the last few decades from less than 30% in the 1960s to currently over 80%. As a result of these improved survival rates, a large and ever growing number of childhood cancer survivors have reached adulthood. A major concern following treatment of childhood cancer is the increased risk of late mortality due to common chronic diseases of mature adulthood observed in the general population. This presentation will provide an overview of the evidence from current large-scale cohort studies investigating cause-specific mortality after treatment for childhood cancer. It will describe the frequency of overall mortality and the risk of mortality due to specific causes of death. Particular attention will be given to the extent to which cause-specific mortality varies by type of childhood cancer and to what extent mortality patterns vary by attained age and time since childhood cancer diagnosis. More survivors are now reaching an age at which, in the general population, the risk of common diseases of mature adulthood increases. This implies that even a small increased risk of mortality relative to that observed in the general population could lead to a substantial excess number of survivors of childhood cancer dying prematurely. Recent large-scale cohort studies with extended follow-up are now starting to report cause-specific mortality risks beyond 40 years of follow-up, i.e. into middle age, and it is becoming evident that the majority of the excess late mortality is attributable to deaths due to second primary cancer and cardiovascular disease. Understanding the long-term risks of mortality is crucial because it provides a basis for counselling long-term survivors, planning future clinical follow-up and deciding on new treatment protocols with the ultimate aim of reducing late mortality without compromising the currently achieved five-year survival rates.

Female fertility in survivors of childhood malignancy
Hamish Wallace
University of Edinburgh, Royal Hospital for Sick Children, UK
16.50 – 17.15, Hall 1C
With 70% of young patients with cancer becoming long-term survivors the issue of fertility outcome has become an issue of great importance (Wallace et al 2012). Female fertility preservation provides significantly different challenges to that for the male (Wallace et al. 2005). Embryo freezing is now a well-established procedure in many centres, but is not available for children who do not have a partner. Cryopreservation using vitrification of mature oocytes has become increasingly successful, but requires the patient to go through a course of hormone stimulation and is therefore not appropriate for children and young girls. Ovarian tissue cryopreservation has the potential advantages of preservation of a large number of oocytes within primordial follicles, it does not require hormonal stimulation when time is short, and is appropriate for the pre-pubertal girl. Disadvantages include the need for an invasive procedure, and the uncertain risk of ovarian contamination in haematological and other malignancies. Ovarian tissue cryopreservation in adult women with later re-implantation has resulted in at least 20 live births worldwide.

We strongly recommend that all young patients with cancer have an assessment made of their fertility prognosis before they commence treatment (Wallace WH et al 2012). We have previously published guidelines for patient selection in young female patients with cancer and in this lecture I will report our practise in a single centre that has offered fertility preservation since 1996. Ovarian cryopreservation was offered to 9% of our patients, and performed in 5%. The procedure was safe and without complications. All but one of our patients who have thus far developed premature ovarian insufficiency were identified pre-treatment using our criteria. More research is required before ovarian tissue cryopreservation in young patients with cancer can be considered to be an established technique available to patients out with IRB approved studies.

References

Late effects of childhood cancer: What are the consequences for long-term survivors and how can they be reduced?
Melissa M Hudson
St. Jude Children’s Research Hospital, Memphis, USA
17.15 – 17.40, Hall 1C

The majority of children and adolescents diagnosed with cancer will become long-term survivors with many potential years of life ahead of them. This growing population is at increased risk for late medical and psychosocial complications (“late effects’) that can adversely affect the quality of their survival and predispose them to early mortality. Late effects account for a high prevalence of chronic health conditions among ageing survivors of paediatric cancers and increase in prevalence with longer time elapsed from cancer diagnosis. Aspects of physical health that may be affected by cancer include growth and development, organ function, fertility and reproductive outcomes, and the risk of secondary carcinogenesis. Similarly, cancer may predispose to a variety of psychosocial sequelae that may negatively impact social competence by hindering educational achievement, vocational and employment opportunities, insurance access, and marriage and social relationships. Early detection and initiation of preventive/ameliorative interventions provide the opportunity to reduce morbidity and mortality associated with cancer-related late effects. Given that many treatment-
related sequelae may not become clinically apparent until the survivor attains maturity or begins to age, the ability of clinicians to anticipate late treatment effects is essential to provide timely interventions to prevent the development and progression of secondary disease and its adverse effects on quality of life. Risk-based survivor care that includes tailored screening, surveillance, and prevention based on the previous cancer, cancer therapy, genetic predispositions, lifestyle behaviours, and co-morbid health conditions is recommended for all survivors. To optimise risk-based survivor care, several groups have organised health screening guidelines based on evidence from the literature linking specific therapeutic interventions with late treatment complications. This presentation will review the scope of long-term health effects after paediatric cancer, the challenges in coordinating long-term survivor care, and health screening guideline resources available to facilitate survivor care.

Discussion
17.40 – 17.50

Molecular stratification and clinical management of adult high-grade glioma

Introduction
Colin Watts
University of Cambridge, UK
16.20 – 16.25, Hall 1B

The complex molecular genetic heterogeneity of adult high-grade glioma has precluded prognostic and predictive risk stratification until relatively recently. Emerging biomarkers are presenting new challenges in terms of their functional utility in the context of a limited therapeutic armamentarium: Why do tests if a patient will get the drug anyway?

This session will illustrate the challenges and opportunities of molecular genetic stratification using anaplastic astrocytoma and glioblastoma in the elderly as model systems. The session will conclude with a review of the importance of accurate sampling to interrogate tumour evolution and response to treatment.

This session is aimed at oncologists, surgeons, specialist nurses and scientists interested in improving our understanding and management of patients with high-grade brain cancer.

Predictive markers for response to adjuvant procarbazine, lomustine (CCNU) and vincristine (PCV) in anaplastic oligodendroglialomas and oligoastrocytomas
Pim French
Erasmus University Medical Centre, Rotterdam, The Netherlands
16.25 – 16.50, Hall 1B

High throughput ‘omics’ data may accelerate the identification of predictive response markers by screening for genes, methylation sites or genetic changes that are associated with clinical outcome. However, most clinical trial samples are fixed in formalin and embedded in paraffin (FFPE) which results in heavily degraded and chemically modified DNA and RNA. To demonstrate that expression profiling is feasible using FFPE tissues, we performed analysis of 55 paired snap frozen (FF)-FFPE samples. We show that differences in mRNA expression levels are retained in FFPE samples. Similarly, we performed paired FF-FFPE analysis using the Infinium HumanMethylation450 beadchip. Our data show that the reproducibility between replicates was high and independent of time in paraffin (>15 years). Expression and methylation profiling therefore is feasible on RNA/DNA isolated from FFPE samples.
We then performed gene expression and methylation profiling samples from the EORTC–26951 clinical trial. This trial examined the effects of adjuvant procarbazine, CCNU and vincristine (PCV) chemotherapy in anaplastic oligodendrogliomas and oligoastrocytomas and demonstrates that adjuvant PCV chemotherapy improves overall survival. However, a subset of patients clearly benefited more from adjuvant PCV than others. Gene expression profiling demonstrates that intrinsic glioma subtypes (i.e. subtypes with similar gene expression profile) are highly prognostic in EORTC26951 and improve outcome prediction when combined with other prognostic factors. Our data also show that tumours assigned to a specific intrinsic subtype, IGS-9, benefit from adjuvant PCV. Methylation profiling demonstrates that the CpG island methylator phenotype (CIMP) status is prognostic for overall survival in the EORTC26951 clinical trial and that methylation on specific sites within the MGMT promoter are correlated to benefit to PCV chemotherapy. In an exploratory analysis, we have also identified 259 CpG sites associated with treatment benefit in this study. Our data demonstrate the power of using high-throughput ‘omics’ in identifying patients that benefit from treatment.

Molecular stratification and clinical management of adult high-grade glioma: Lessons from the elderly trials
Michael Weller
University Hospital Zurich, Switzerland
16.50 – 17.15, Hall 1B
Age has been identified as a strong negative prognostic factor for patients with anaplastic gliomas and glioblastoma decades ago. Population-based studies in Europe and the US indicate that elderly patients with high-grade gliomas continue to be treated less intensively than younger patients. Notably biopsy is more often the first surgical intervention and elderly patients receive salvage therapies less frequently. Based on recent randomised trials, new standards of care have emerged in the elderly. The initial diagnostic work-up should include the assessment of the O6-methylguanine DNA methyltransferase (MGMT) gene promoter status by methylation-specific PCR. Patients with MGMT promoter-unmethylated glioblastoma should probably be treated with hypofractionated radiotherapy e.g. 15 x 2.66Gy to a total dose of 40Gy. Patients with MGMT promoter-methylated glioblastoma should no longer be treated with radiotherapy alone, but rather with temozolomide at 200mg/m² probably until progression or for 12 cycles. Whether temozolomide should be administered alone as initial therapy and radiotherapy be deferred, or combined with hypofractionated radiotherapy up-front, remains a matter of debate. An ongoing NCIC/EORTC intergroup trial investigates combined hypofractionated radiotherapy and concomitant and adjuvant temozolomide chemotherapy with hypofractionated radiotherapy in elderly patients with glioblastoma. This trial will inform about the magnitude of benefits derived from temozolomide in addition to radiotherapy by MGMT status. New trial concepts of the EORTC focus on the addition of the vascular endothelial growth factor (VEGF) antibody, bevacizumab, to these current standards of care since retrospective studies suggest a preferential clinical role for VEGF inhibition in the subpopulation of the elderly. This concept is currently explored in a Swiss phase II trial (ARTE). Meanwhile, molecular studies have provided the first findings which may explain the poor outcome in the elderly, beyond the general issue of less intensive treatment. The most important finding in this regard is the virtual absence of isocitrate dehydrogenase (IDH) mutations in elderly patients with anaplastic astrocytoma and glioblastoma.
Intra-tumour heterogeneity reflects cancer evolutionary dynamics: Implications for patient stratification

Colin Watts
University of Cambridge, UK
17.15 – 17.40, Hall 1B

Gliomas are characterised by genetic instability and complex evolutionary dynamics. Histopathological diversity results in different clinical phenotypes, whose common feature is the rapid emergence of treatment resistance as a result of environmental selection pressures generated by radiotherapy and chemotherapy.

Recent models of gliomagenesis point to sub-ependymal neural stem cells (NSCs) as a putative cell of origin for astrocytic tumours and it has been shown that the stepwise pre-malignant loss of tumour suppressors p53, NF1 & PTEN\(^1,2\) leads to the development of an aggressive disease phenotype characterised by resistance to genotoxic injury.\(^3,4\) Although these observations reflect specific aspects of the clinical and biological diversity seen in patients, the human disease observed at presentation represents a complex clonal environment. In this context, the maintenance and growth of the cancer may depend on diverse tumorigenic cell populations that are distinct from any cell of origin.\(^5,6\)

To interrogate genetic and clonal diversity we have developed fluorescence-guided multiple sampling (FGMS) that permits real-time spatially segregated tumour sampling during surgery allowing reconstruction of tumour phylogeny\(^7,8\). We have applied FGMS to glioblastoma to describe intra-tumoural heterogeneity, clonal diversity and infer phylogenetic architecture. Analysis of therapeutic responsiveness reveals diverse patterns within an individual tumour. Together these data reveal novel insights into the ontogeny, growth and response to treatment of glioblastoma at the level of the individual patient.


Discussion
17.40 – 17.50
‘Real world’ data: Opportunities and challenges

Introduction
David Ford
Swansea University, UK
16.20 – 16.25, Room 11

Recent years have brought many calls for the optimisation of data for research, with the intention of deriving maximal societal benefit from the quality, volume and accessibility of ‘real world’ data being collected routinely by the National Health Service (NHS). As well as traditional uses in epidemiology and health services research real world data can supplement information that would previously have required separate data collection. This session will identify and present the developing field of using real world data in novel ways: To conduct pragmatic randomised trials, to assist with recruitment to studies and to support follow up of large cohorts.

Impact of ‘real world data’ on cancer patient outcomes and care
Anna Gavin
Northern Ireland Cancer Registry, Queen’s University Belfast, UK
16.25 – 16.50, Room 11

How can we best address patient questions about achieving the best treatment, their predicted survival, likely side effects and quality of life? This, while answering questions about achievement of standards and costs and coping with increasing cancer numbers fuelled by an ageing population, spiralling costs and interest in improving outcomes. Data collection is expensive yet patient activity generates millions of data items each year which are accessible electronically. In recent years linkages of routine data on cancer patients and their use of services has improved the knowledge available to service providers, researchers and patients. Examples of such research will be presented.

The patient input to research is getting stronger now with the National Cancer Survivorship initiative which has documented cancer patients’ wellbeing in Patient Reported Outcome Measures (PROMS), and integration of patients in research funding allocation committees, research steering groups, and outcome dissemination, the challenge is how to empower patients further. Linkages of lifestyle, disease, molecular and service data will provide a complete picture for determination of individual risks and best treatments. Prevalence work dissecting the two million (soon to be three million) cancer survivors to determine where patient live, how long since diagnosis etc. will facilitate more patient centred services and research opportunities.

Areas for discussion include whether patients benefit from this use of their personal data? Whether subgroups can be identified who are neglected in services or research? And is the patient’s voice heard?

Title TBC
Eva Morris
St James’ University Hospital, Leeds, UK
16.50 – 17.15 , Room 11

Title TBC
Tim Hubbard
Wellcome Trust sanger Institute, Cambridge, UK
17.15 – 17.40 , Room 11
Discussion
17.40 – 17.50

Re-shaping clinical practice in neuroendocrine tumours (NETs)

Introduction
John Primrose\textsuperscript{1} and Juan Valle\textsuperscript{2}
\textsuperscript{1}University of Southampton, UK and \textsuperscript{2}The Christie NHS Foundation Trust, Manchester, UK
16.20 – 16.25, Room 3A

Neuroendocrine tumours (NETs) are considered rare tumours; however, due to their indolent course they are the second commonest gastrointestinal (GI) malignancy by prevalence. Improved understanding of the biology of NET behaviour twinned with imaging and therapeutic advances are changing the paradigm of clinical practice. In this session we will focus on emerging molecular insights gained from circulating biomarkers; explore the concept of ‘Theranostics’ (molecular imaging leading to therapy) when applied to NETs and review the relative merits of systemic therapies with specific attention to optimal use and sequencing of available treatments for patients with advanced disease.

Integrated genomic analysis and application of single cell and circulating free DNA sequencing in NET management

Chrissie Thirlwell
University College London Cancer Institute and Royal Free Hospital NET Unit, London, UK
16.25 – 16.50, Room 3A

Neuroendocrine tumours (NETs) are a clinically and genetically heterogeneous group of cancers with markedly different clinical outcome depending on the primary site and grade of tumour. Due to the rarity of NETs, previous genomic studies have included small sample sizes, often originating from mixed primary sites.

My group has undertaken the first large scale integrated genomic analysis of pancreatic and intestinal NETs including exome sequencing, genome-wide DNA methylation analysis, RNA expression and copy number analysis.

This analysis has identified disruption of the Wnt signalling and neurodevelopmental pathways in NET development. DNA methylation biomarkers (tissue-based and circulating) have been identified which differentiate between normal tissue and NETs and also between grade of NET. This includes the identification of promoter methylation of \textit{RASSF1} as a candidate pathogenic driver; whilst analysis of circulating free DNA has identified \textit{RASSF1} hypermethylation in gastrointestinal GI NET patients relative to normal controls.

Gene ontology analysis has identified genes in pathways associated with everolimus resistance to be differentially methylated in tumour tissue. This is of particular significance following the introduction of everolimus therapy in pancreatic NETS with on-going phase III trials in intestinal and bronchial NETs.

Co-workers at UCL recently identified and validated circulating tumour cells (CTCs) as a prognostic biomarker in NET patients with metastatic disease. We have since isolated and sequenced DNA from single NET CTCs. Analysis of CTCs can teach us about mechanisms of metastatic spread and also determine the how resistance to systemic therapy develops. Alongside this we have also quantified and sequenced circulating free DNA in NET patients. In future, analysis of this ‘liquid biopsy’ will enable us to truly personalise cancer therapy for NET patients.
Theranostics: From molecular imaging using PET/CT to personalised therapy of over 1100 patients with neuroendocrine tumours (NETs)
Harshad Kulkarni
ENETs Centre of Excellence, Zentralklinik Bad Berka, Germany
16.50 – 17.15, Room 3A

$^{68}$Gallium is a positron emitter ($T_{1/2}$ 68 min) which can be produced from a generator in a convenient, ‘in-house’ preparation and used for labelling of peptides e.g. somatostatin analogues (SA) like DOTATOC/DOTANOC/DOTATATE for molecular imaging of SSTR expressing tumours. Since 2004, we have performed over 8500 $^{68}$Ga-PET/CT studies in patients with neuroendocrine tumours (NETs) and have established SSTR PET/CT as the new gold standard for imaging G1 and G2 NET (staging, restaging, therapy response evaluation and detection of unknown primary NET).

The same peptides can be labelled with $^{177}$Lutetium or $^{90}$Yttrium for peptide receptor radiotherapy (PRRT), a form of personalised treatment (theranostics approach). A German multi-institutional registry study with prospective follow up in 450 patients indicates that PRRT is an effective therapy for patients with G1–2 neuroendocrine tumours with a survival advantage of several years compared to other therapies and only minor side effects. Median overall survival (OS) of all patients from the start of treatment was 59 months. Median progression-free survival (PFS) measured from last cycle of therapy accounted to 41 months. Median PFS of pancreatic NET was 39 mo. Similar results were obtained for NET of unknown primary (median PFS: 38 months) whereas NET of small bowel had a median PFS of 51 months. Side effects like grade 3-4 nephro- or haematotoxicity were observed in only 0.2% and 2% of patients, respectively. Fractionated PRRT with lower doses of radioactivity given over a longer period of time (Bad Berka Concept) results in excellent therapeutic responses. By this approach, severe haematological and/or renal toxicity can be avoided and quality of life/clinical symptoms can be significantly improved.

The concept of theranostics has now been translated to other malignancies as well (e.g. prostate cancer) and current state and future perspectives of this fascinating approach will be discussed.

Systemic therapy options for NETS: When and what
Ramón Salazar
Institut Català d’Oncologia, L’Hospitalet de Llobregat, Barcelona, Spain
17.15 – 17.40, Room 3A

Well-differentiated NETs (WDNETs) are a subset of tumours with slow growth and sometimes relatively indolent behaviour. STZ based chemotherapy has been the only standard systemic therapy for pancreatic NETs (pNETs) for decades.

Recently the mTOR inhibitor, everolimus, has shown to be efficacious in well differentiated NETs. Everolimus 10mg/day, as compared with placebo, significantly prolonged progression-free survival among patients with progressive advanced pancreatic neuroendocrine tumors and was associated with a low rate of severe adverse events (RADIANT-3 study). Results published from this study showed a median progression-free survival of 11.0 months. This study included patients with advanced, low-grade or intermediate grade pNET with radiologic progression within the previous 12 months. Synchronously, sunitinib has shown simillar results in the same population. Patient characteristics, safety profile, final sample size and conduct of the trial design and statistics differ between trials but both drugs have been recently approved for its use in advanced pHNETs in US by the FDA and in Europe by the EMEA.

STZ-5-FU, is the current standard of care for advanced pNETs in the European Union (ENETS guidelines;
Neuroendocrinology 2012). Everolimus and sunitinib are also available and reimbursed in many countries for the same population. One can speculate on a number of clinical variables that may help guide the right treatment sequence and these will be reviewed but the lack of valid predictors of response for one or another drug makes it impossible to choose the optimal sequence for every patient. A randomised study is needed to have a clear knowledge about the best sequence of administration of these new targeted therapies and chemotherapy. A concept and design for such a trial is underway and will be presented. The SEQTOR trial aims to randomise patients with advanced pancreatic pNETs to receive STZ-5FU chemotherapy upfront and everolimus upon progression or the inverse sequence. In addition, a large ancillary biologic study exploring putative predictive and monitoring biomarkers will also be performed, with the idea to find specific biomarkers of response that may help individualise treatment decision in the future.

Discussion
17.40 – 17.50

Smarter surgery for better cancer outcomes

Introduction
Dion Morton
University of Birmingham, UK
16.20 – 16.25, Room 3B

Surgical research is entering a new era, and this session will illustrate how partnerships between surgeons and other researchers have improved our understanding of cancer and how to treat it. Talks are aimed at oncologists, surgeons, methodologists and scientists interested in the connections that can be established between surgery and other cancer disciplines.

The first presentation will consider how surgery to remove tumour tissue provides a unique opportunity for biomarker and drug discovery research, with a focus on breast cancer window trials. We will then explore mutually beneficial research partnerships between surgeons and oncologists, such as the use of neoadjuvant treatment to reduce the extent and burden of a surgical procedure. The third talk will review what makes prospective research involving a surgical intervention complex to design and deliver, and how to get around these challenges.

The session will conclude with a discussion about how the surgical community and other cancer disciplines can interact effectively to build future partnerships for research.

Smarter surgery for better cancer outcomes: Leading the way with breast cancer
Alastair M Thompson
Dundee Cancer Centre, UK
16.25 – 16.50, Room 3B

Breast cancer exemplifies a smarter approach to improving surgical outcomes in oncology. Historically, the move from radical mastectomy, through mastectomy to breast conservation has recently been matched with sentinel node biopsy replacing axillary node clearance for most women. Oncoplastic approaches have improved cosmetic outcomes and tailored neoadjuvant approaches allow wide excision where mastectomy would have been required.

The neoadjuvant approach has been developed to allow comparisons of chemotherapy, endocrine therapy and more
recently targeted therapy regimens. Indeed neoadjuvant drug therapy has become standard of care to downsize primary breast cancers over 2cm in size, not purely for locally advanced breast cancer. The neoadjuvant setting can also complement the adjuvant clinical setting with 20-fold fewer patients required to generate comparable data.

The few days or weeks prior to surgery offer a ‘window of opportunity’ to examine the *in vivo* effects in women of one or more drugs. Such studies can examine on target, anticancer and systemic effects in a range of tumour, normal and blood samples. Pre-treatment, on-treatment and post-treatment tissues can be analysed using a range of biomarker techniques. This approach can be useful not only to test hypotheses but also to generate data requiring further *in vitro* and *in vivo* study.

Smarter surgery in breast cancer has evolved into multidisciplinary interactions overcoming many challenges in research design and delivery. Similar approaches to other anatomical surgical sites present challenges requiring interdisciplinary collaboration, but offer substantial opportunities for therapeutic development with great potential to improve patient care.

**Surgeons and oncologists: Optimising surgery within multimodality treatment**

David Sebag-Montefiore¹ and Simon Bach²

¹University of Leeds, UK and ²Queen Elizabeth Hospital, Birmingham, UK

16.50 – 17.15, Room 3B

Rectal cancer is an excellent example of a disease in transition. Early diagnosis through screening increases the opportunity to evaluate novel strategies that preserve the organ and its function. The challenge is to retain excellent oncological outcomes.

Clinical trials in locally advanced disease established that the addition of radiotherapy to radical resection results in a significant reduction in local recurrence. Prospective studies of both preoperative radiological staging and histopathological assessment have dramatically improved our ability to appropriately select patients for multimodal therapy. Currently rectal cancer is associated with rapidly reducing disease-associated mortality, but treatment related morbidity and mortality unfortunately remain high. The majority of long term toxicity is caused by radical surgery.

Bowel cancer screening provides us with an opportunity to re-evaluate the therapeutic strategy for rectal cancer. Radical surgery achieves complete rectal and mesorectal excision, providing definitive information about T stage and local nodal metastasis. If no involved nodes are found then there is little risk of regional recurrence and diminished risk of systemic relapse. The majority of T1 and T2 rectal cancers, (80-85%), are limited to the bowel wall without lymph node involvement. Routine lymph node dissection in these patients is over-treatment and could potentially be avoided.

An alternative is to target only the small area of bowel directly affected by the tumour, preserving the remaining rectum and its function. The primary tumour may be treated by either excision or radiotherapy. The challenge of comparing the current standard of care with an organ preserving approach within clinical trials will be discussed including our experience with a Cancer Research UK funded trial (TREC) addressing this question. We will also discuss approaches to evaluate the different approaches to organ preservation.

**Smarter trial designs in surgical oncology**

Jane Blazeby

University of Bristol, UK

17.15 – 17.40, Room 3B
The overall aim of this talk is to consider optimal designs for successful randomised clinical trials (RCTs) in surgical oncology. Specifically it will outline pragmatic trial designs and the need for pilot or feasibility work for efficient and effective trial conduct and delivery.

There are several funding streams for RCTs in surgical oncology and the key to success is to design high quality studies that answer questions of importance to patients and the NHS. Recent investments from the Royal College of Surgeons of England into surgical trials centres and from the MRC into Hubs for Trials Methodology Research combined with National Institute of Health Research and Cancer Research UK funding streams means that there are unprecedented opportunities for surgeons and trials methodologists to work together to design and conduct multi-centre pragmatic trials.

Key features of pragmatic trial design include: i) broad participant, surgeon and centre inclusion, so that results are generalisable; ii) evaluation of interventions with sufficient stability to warrant multi-centre assessment; and, iii) selection of outcome measures that are of importance to patients and the health service. These issues are unfamiliar to surgeons therefore feasibility and pilot work is recommended before or part of a main trial.

The strengths and weaknesses of external pilot RCTs, standalone feasibility studies and main trials with an integrated internal pilot and pre-agreed progression criteria will be presented. The value of feasibility and pilot work to optimise recruitment, develop surgical interventions and create a functional multi-disciplinary team to deliver the main trial will be considered with examples.

**Discussion**
17.40 – 17.50

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**Targeting the epigenome**

**Introduction**
Robert Brown
Imperial College London, UK
16.20 – 16.25, Hall 1A

Tumours show widespread aberrant epigenetic changes, leading to changes in expression of genes involved in all the hallmarks of cancer. These epigenetic changes can be reversed, at least temporarily, using small molecule inhibitors of maintenance of the epigenetic state. Some first generation epigenetic therapies are now registered for use in certain haematological malignancies. Our increased understanding of mechanisms controlling the epigenome and its aberrant control in cancer, provide exciting opportunities for novel anticancer approaches. This session will cover some of the emerging epigenetic targets and drug discovery around these targets.

**Working together to exploit a rich seam of novel epigenetic targets for cancer**
Chas Bountra
University of Oxford, UK
16.25 – 16.50, Hall 1A

During my presentation, I will discuss:

- How we are pooling the expertise and infrastructure of several big pharmaceutical companies, with disease and clinical expertise, and patients resources in academia, to accelerate novel target identification.
• Novel epigenetic targets which are worth further exploration.
• How these efforts are facilitating science and proprietary programmes, including the creation of new biotechs.
• Our plans to establish a nationwide, human disease platform for novel epigenetic target prioritisation.

**Cancer epigenetics: From mechanism to therapy**

*Mark Dawson*
Cambridge Institute for Medical Research & Wellcome Trust and Cancer Research UK Gurdon Institute, University of Cambridge, UK
16.50 – 17.15, Hall 1A

Chemical modifications of histones and DNA occurs through highly conserved enzymes, and these modifications are in turn ‘read’ by chromatin adaptor proteins. The information conveyed by these processes plays a critical role in the regulation of all DNA based processes such as transcription, DNA repair and replication. Consequently, when these epigenetic enzymes or readers are mutated the results are often devastating and lead to the induction and/or maintenance of various cancers. Understanding the molecular mechanisms by which these epigenetic regulators contribute to cancer may provide an opportunity to target these factors with novel epigenetic therapies. We have recently identified a previously unrecognised nuclear role for JAK2 as a histone tyrosine kinase and demonstrated a novel signalling pathway by which JAK2 directly regulates chromatin structure and transcription in mammalian cells (Dawson et al; Nature 2009). Our current research has centred on deciphering the molecular mechanisms by which MLL-fusions regulate transcriptional programmes involved in leukaemogenesis. We have identified the BET proteins, in particular BRD4, as components of large macromolecular chromatin complexes associated with MLL-fusions and have demonstrated that small molecules that target these epigenetic readers are effective therapeutic agents in MLL-fusion leukaemia (Dawson et al; Nature 2011).

**Targeting EZH2 in haematological malignancies**

*Patrick Trojer*
Constellation Pharmaceuticals, Cambridge, USA
17.15 – 17.40, Hall 1A

Lysine methyltransferases and demethylases were identified as transcriptional co-regulators functioning by either preserving particular chromatin methylation states or by controlling placement and removal of histone lysine methylation marks to promote dynamic changes in gene expression. The development of small molecule methyltransferase and demethylase inhibitors provides a novel approach to affect the regulation of transcription, and thus potentially allowing interference with aberrant transcriptional programs as observed, for instance, in cancer.

Enhancer of Zeste Homolog 2 (EZH2), the major histone H3 lysine 27 (K27) methyltransferase, is widely implicated in tumour progression. The presence of a recurrent mutation of single residues in the EZH2 catalytic domain in germinal center B-cell like diffuse large B-cell lymphoma (GCB-DLBCL) and follicular lymphoma suggests that these cancers might be dependent on altered EZH2 molecular function. Small molecule inhibitors of EZH2 have recently demonstrated efficacy in GCB-DLBCL models and thus provide a new therapeutic approach to treat human lymphomas, especially cases with activating EZH2 mutations.

Constellation has identified, characterised and optimised potent, selective, reversible, orally bioavailable EZH2 small molecule inhibitors. We find that pharmacological inhibition of EZH2 causes selective cell viability defects across a
number of haematological disease models beyond GCB-DLBCL harbouring EZH2 mutations. Genome-wide mapping of EZH2 and H3K27me3 sites in the absence and presence of the compound revealed that the EZH2 inhibitor caused significant changes to the local chromatin modification landscape, however only a subset of these alterations translated into gene expression changes. Various biological contexts that depend on EZH2 catalytic activity will be discussed.

Discussion
17.40 – 17.50

The issues with tissues

Introduction
Mairead MacKenzie
Independent Cancer Patients’ Voice, UK
16.20 – 16.25, Room 4

Independent Cancer Patients’ Voice (ICPV) invites professional and lay delegates, who are interested in the donation, collection and use of human tissue in cancer research, to join us to discuss current and potential needs for this tissue and possible barriers to successful cancer biobanking.

Presentations about aspects of tissue use in Europe and UK and the importance of lay involvement will be followed by a lively discussion when audience participation will be actively encouraged. The aim is to illustrate what tissue is needed, show the value of lay involvement and help reduce unnecessary barriers to effective cancer biobanking.

The critical need for longitudinal tissue and blood sample collection in cancer research
Mariam Jamal-Hanjani1 and Matthew Krebs2
1University College London, UK and 2The University of Manchester, UK
16.25 – 16.45, Room 4

The collection of human tissue and blood samples is of utmost importance for cancer research and delivering personalised medicine. There is increasing evidence to support inter- and intra-tumour heterogeneity and evolution of disease over time, particularly in acquiring resistance to systemic therapy. Longitudinal collection of tissue is therefore essential to fully interrogate the evolving tumour genomic landscape and to identify targets for therapeutic intervention. Analysis of circulating tumour cells and cell-free DNA, acquired from a simple blood test, may also represent tumour heterogeneity, offering a minimally invasive means for tumour monitoring and has the potential to become an invaluable tool in the clinic for personalised therapy.

Challenges in using samples for clinical research: A pan-European perspective
Jacqueline Hall
Formerly Head of Translational Research Unit, European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium
16.45 – 17.05, Room 4

With an increased understanding of the molecular heterogeneity of cancer, access to samples is now becoming critical for clinical research and cancer trials. However, challenges can arise in collection, storage and use of samples in research due to a complex or unclear regulatory environment and varying local governance rules of individual institutes. In this talk key
challenges will be discussed including examples and recommendations on how we can move forward will be reviewed.

**Consent: Asking the question?**

Hilary Stobart\(^1\) and Helen Bulbeck\(^2\)

\(^1\)Member of PPI Advisory Group and Volunteer, Nottingham Health Science Biobank, Nottingham University Hospitals NHS Trust, UK; \(^2\)Brainstrust, UK

17.05 – 17.25, Room 4

Nottingham Health Science Biobank is keen to involve patients, carers and members of the public in different aspects of its work, including innovative consent pathways. This brings both challenges and rewards.

**Discussion**

Chaired by Bridget Wilkins

Guy’s and St. Thomas’s Hospital, London, UK

17.25 – 17.50
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Programme at a glance

Workshops

08.00 – 08.45  BACR educational workshop: Relative merits of ctDNA and CTCs as circulating biomarkers to aid cancer patient management
   Hosted by Jacqui Shaw¹, Caroline Dive², Ged Brady², Nitzan Rosenfeld³, ¹University of Leicester, UK, ²Cancer Research UK Manchester Institute, Manchester, UK, ³Cancer Research UK Cambridge Institute, UK

08.00 – 09.00  Charles River workshop: Cutting edge cancer modelling using the NGS mouse
   Hosted by Charles River UK Ltd and The Jackson Laboratory
   Tea, coffee and pastries will be provided

Clinical Trials Showcase part 1

Hosted by Matt Seymour, NIHR Cancer Research Network, Leeds, UK

09.00 – 09.20  A randomised clinical trial of chemotherapy compared to chemotherapy in combination with cetuximab in KRAS wild-type patients with operable metastases from colorectal cancer: The new EPOC study
   John Bridgewater, University College London Hospitals NHS Foundation Trust, UK

09.20 – 09.40  A multicenter phase III randomised double-blind placebo controlled trial of pravastatin added to first-line standard chemotherapy in patients with small cell lung cancer (SCLC)
   Michael Seckl, Imperial College London, UK

Plenary lecture

Chaired by Richard Marais, Cancer Research UK Manchester Institute, UK

09.40 – 10.20  Defective DNA strand break repair, genome instability and cancer
   Stephen C West, Cancer Research UK London Research Institute, UK

Poster session B (odd numbers), refreshment break, networking and exhibition viewing

10.20 – 11.20  For further details, please refer to the Poster Abstracts book or USB stick, and the exhibition section in this book

Symposia

11.20 – 12.50  Clinical decision support systems
   Hosted by Willie Hamilton, University of Exeter Medical School, UK

11.20 – 12.50  Latest developments in radiotherapy for breast cancer
   Hosted by Alastair M Thompson, Dundee Cancer Centre, UK
11.20 – 12.50  The bacteriome and cancer
Room 3B  Hosted by Elaine Holmes, Imperial College London, UK

11.20 – 12.50  We need to talk about clonal diversity
Room 11  Hosted by Mel Greaves, The Institute of Cancer Research, London, UK

Networking, exhibition viewing, poster viewing and lunch
12.50 – 13.50  For further details, please refer to the Poster Abstracts book or
Hall 2  USB stick, and the exhibition section in this book

Commercial workshop
13.00 – 14.00  Headlines of International Congresses in 2013
Room 11  Sponsored by Roche Products Limited
Lunch will be provided in the room

Poster session B (even numbers)
13.30 – 14.30  For further details, please refer to the Poster Abstracts book or
Hall 2  USB stick, and the exhibition section in this book

Proffered paper sessions
14.30 – 16.00  Cancer awareness and population studies
Hall 1B  Hosted by Jane Wardle, University College London, UK
14.30 – 16.00  The cancer cell and model systems II
Room 11  Hosted by Julian Downward, Cancer Research UK London Research Institute, UK
14.30 – 16.00  Diagnosis and therapy
Room 3A  Hosted by Patrick Johnston, Queen’s University Belfast, UK
14.30 – 16.00  Radiotherapy and radiobiology
Hall 1A  Hosted by Diana Tait, The Royal Marsden NHS Foundation Trust and Dean, The Royal College of Radiologists, London, UK

Workshops
14.30 – 16.00  Improving the design and reporting of studies on early diagnosis across all cancer types
Room 3B  Hosted by Richard Neal, Bangor University, Wrexham, UK
14.30 – 16.00  “What I’d like to talk to you about now is a clinical trial…”
Room 4  Hosted by Alison Ames and Chris Hough, Northern Networks Facilitator Group, UK
Networking, exhibition viewing, poster viewing and refreshment break

16.00 – 16.20  For further details, please refer to the Poster Abstracts book or Hall 2 USB stick, and the exhibition section in this book

Parallel sessions

16.20 – 17.50  Application of nanotechnology to oncology
Room 11  Hosted by Katherine Vallis, Gray Institute for Radiation Oncology & Biology, Oxford, UK

16.20 – 17.50  Autophagy, senescence and cell death
Room 3A  Hosted by Daniel Murphy, University of Glasgow Institute of Cancer Sciences and Cancer Research UK Beatson Institute, UK

16.20 – 17.50  Clinical application of translational research in breast cancer
Hall 1A  Hosted by John Yarnold, The Institute of Cancer Research, London, UK

16.20 – 17.50  Immunotherapy of childhood cancer
Hall 1C  Hosted by John Anderson, Institute of Child Health, University College London, UK

16.20 – 17.50  Refractory breathlessness: Mechanisms and management
Room 4  Hosted by Miriam Johnson, Hull York Medical School, UK

16.20 – 17.50  The ‘end game’ for tobacco control in the UK: Key priorities for science and policy to reduce smoking
Room 3B  Hosted by Linda Bauld, University of Stirling, UK

16.20 – 17.50  The importance of knowing which way is up – the role of polarity in tumour suppression
Hall 1B  Hosted by Buzz Baum, University College London, UK

Networking and break

17.50 – 18.00  Registration Area

Clinical Trials Showcase part 2

Hosted by Matt Seymour, NIHR Cancer Research Network, Leeds, UK

18.00 – 18.20  Involved field radiotherapy versus no further treatment in patients with clinical stages IA and IIA Hodgkin lymphoma (HL) and a negative PET scan after 3 cycles ABVD. Results of the UK NCRI RAPID trial
Hall 1A  John Radford, The University of Manchester and The Christie NHS Foundation Trust, UK
18.20 – 18.40
Hall 1A Randomised double-blind phase III trial of cediranib (AZD 2171) in relapsed platinum sensitive ovarian cancer: Results of the ICON6 trial
Jonathan A Ledermann, Cancer Research UK and University College London Cancer Trials Centre, UK

Plenary lecture
Chaired by Malcolm Mason, Cardiff University, UK
18.40 – 19.20
Hall 1A The application of translational science in non-small cell lung cancer (NSCLC): Successes, failures and pitfalls
Frances A Shepherd, Princess Margaret Hospital and University of Toronto, Canada

Conference dinner and party (ticketed event)
20.00 onwards The Echo Arena, BT Convention Centre
Limited tickets are available for this event. Please go to the onsite payments desk to reserve your place
Defective DNA strand break repair, genome instability and cancer
Stephen C West
Cancer Research UK London Research Institute, UK
09.40 – 10.20, Hall 1A

All living organisms feature DNA repair pathways that safeguard the integrity of the genome, and mutations in proteins that mediate key events in DNA repair have been linked to genome instability and tumorigenesis. One particularly dangerous form of DNA damage occurs when the chromosomes suffer double-strand breaks and these need to be repaired efficiently in order to avoid DNA translocations or partial chromosome loss. Mutations in tumour suppressors such as BRCA2, PALB2, or BLM affect the efficiency of DNA repair by a process known as homologous recombination.

Many of the key steps of recombination have now been reconstituted with purified proteins and defined DNA substrates, leading to a good understanding of the molecular mechanism of this repair process. In particular, we have purified the BLM protein (defective in the cancer-prone disease known as Bloom’s Syndrome), the BRCA2 (FANCD1) and PALB2 (FANCN) tumour suppressors (also mutated in some cases of Fanconi anemia), and the newly discovered FANCP protein, also known as SLX4, and have initiated structure-function analyses to elucidate their molecular functions. How these proteins process DNA, and how they are regulated and controlled to direct the outcome of recombinational repair is now revealing unexpected insights that extend our understanding of efficient DNA repair and tumour avoidance.

The application of translational science in non-small cell lung cancer (NSCLC): Successes, failures and pitfalls
Frances A Shepherd
Princess Margaret Hospital and University of Toronto, Canada
18.40 – 19.20, Hall 1A

The identification of key genetic pathways and mutations in NSCLC will be critical to furthering our understanding of this malignancy and to developing new molecularly targeted therapies. This presentation will focus on the complexity of genetic mutations in lung cancer using select mutations as examples.

KRAS frequently is mutated in NSCLC. The LACE-Bio meta-analysis involving 1721 patients reported modestly worse outcome (HR 1.09, p=0.39; adenocarcinoma HR 1.03, p=0.93). However, overall, KRAS mutation was not predictive of differential benefit from chemotherapy with the exception of Codon-13 mutations. Data also are conflicting with respect to the ability of KRAS mutation to predict outcome in patients treated with EGFR TKIs and no study has shown that KRAS is predictive for EGFR monoclonal antibody therapy.

Biomarker studies of EGFR mutation are complex, and results vary depending on whether the EGFR TKI is compared to placebo, added to other treatments or compared to other treatments. Clearly EGFR driver mutations on exons 19 and 21 predict for very high response rates to TKIs, but despite initially dramatic responses, all patients with NSCLC relapse and die of disease. Examination of the downstream pathway markers has led to strategies to delay or overcome resistance through combination of agents or new agents in the same class designed to overcome or bypass resistance. MET inhibitors, angiogenesis inhibitors are under study, and second and third-generation EGFR inhibitors are being tested and even approved.

The identification of EML4-ALK mutations led to the rapid approval of crizotinib based on Phase II trials alone, and now Phase III post-commitment studies have confirmed this activity in trials comparing crizotinib to chemotherapy. Despite
approval <2 years ago, several second generation ALK inhibitors are in development, and have demonstrated activity. The addition of HSP90 targeting agents also may be particularly useful in the setting of ALK mutations resistant to crizotinib.
A randomised clinical trial of chemotherapy compared to chemotherapy in combination with cetuximab in KRAS wild-type patients with operable metastases from colorectal cancer: The new EPOC study

John Primrose¹, Stephen Falk², Meg Finch-Jones³, Juan Valle⁴, Joanne Hornbuckle⁵, Mark Peterson⁵, Ajith Siriwardena⁶, David Cunningham⁷, Graeme Poston⁸, Tim Maughan⁹, Myrردن Rees¹⁰, Derek O’Reilly¹¹, Elizabeth Dixon¹², Louisa Little¹², Wendy Wood¹², Megan Bowers¹², Louise Stanton¹², Tom Maishman¹², Siân Pugh¹, John Bridgewater¹²

¹University Hospital Southampton, Southampton, UK, ²Bristol Haematology and Oncology Centre, Bristol, UK, ³University Hospitals Bristol, Bristol, UK, ⁴The Christie NHS Foundation Trust, Manchester, UK, ⁵Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK, ⁶Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK, ⁷The Royal Marsden Hospital NHS Foundation Trust, London, UK, ⁸Aintree University Hospital NHS Foundation Trust, Liverpool, UK, ⁹Gray Institute for Radiation Oncology and Biology, University of Oxford, Oxford, UK, ¹⁰Hampshire Hospitals NHS Foundation Trust, Basingstoke, UK, ¹¹The Pennine Acute Hospitals NHS Trust, Manchester, UK, ¹²University of Southampton Clinical Trials Unit, Southampton, UK, ¹³University College London Hospitals NHS Foundation Trust, London, UK

09.00-09.20, Hall 1A

Background
Liver resection is the only curative treatment for colorectal liver metastases (CRLMs). The EPOC trial showed an 8.1% PFS improvement at 3 years in eligible patients given FOLFOX before and after liver resection over surgery alone. The New EPOC trial evaluates the benefit of cetuximab, an EGF receptor antibody, in addition to standard chemotherapy in patients with operable CRLM.

Method
Eligible patients were KRAS wild-type with operable or borderline operable CRLM. Primary tumour in situ was permitted. Patients were randomised to receive a fluoropyrimidine and oxaliplatin +/- cetuximab for 12 weeks before, then 12 weeks following surgery. Patients with prior oxaliplatin exposure could receive irinotecan and 5-fluorouracil. The primary endpoint was PFS (progression free survival).

Results
In November 2012, the Independent Data Monitoring Committee and Trial Steering Committee recommended closure of the trial. A total of 272 patients had been randomised and 112 of the 212 required events observed. PFS was significantly worse in the cetuximab arm (14.1 vs 20.5 months, HR 1.49 95%CI (1.04, 2.12) p=0.030. Pre-operatively a better response was observed in the cetuximab arm (42.0% vs 50.0% relative reduction in the size of the 4 largest lesions). Rates of surgical resection and delivery of chemotherapy both pre and post-operatively were equivalent between the arms.

Conclusion
The addition of cetuximab to chemotherapy in patients with operable or borderline operable CRLM increases the pre-operative response rate in line with prior studies. Despite this the PFS is significantly worse in the cetuximab treated patients. In this setting the presence of KRAS wild-type is insufficient to predict benefit. Further translational work is needed to determine the nature of the interaction leading to this unexpected outcome and also to determine whether there may be circumstances in which cetuximab may be of benefit.
A multicenter phase III randomised double-blind placebo controlled trial of pravastatin added to first-line standard chemotherapy in patients with small cell lung cancer (SCLC)

Michael Seckl1, Christian Ottensmeier2, Mike Cullen3, Peter Schmid4, Lindsay James5, Christina Wadsworth5, Hannah Farrant1, Dakshinamoorthy Muthukumar6, Joyce Thompson1, Susan Harden5, Gary Middleton5, Kate Fife10, Barbara Crosse11, Paul Taylor12, Iftekhar Khan5

1Imperial College London, London, UK, 2Southampton University, Southampton, UK, 3Queen Elizabeth Hospital Birmingham, Birmingham, UK, 4Brighton and Sussex Medical School, Brighton, UK, 5Cancer Research UK and University College London CTC, London, UK, 6Colchester University Hospital NHS Foundation Trust, Colchester, UK, 7Heart of England NHS Trust, Birmingham, UK, 8Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK, 9Royal Surrey County Hospital, Guildford, UK, 10Peterborough and Stamford Hospitals NHS Foundation Trust, Peterborough, UK, 11Calderdale and Huddersfield NHS Foundation Trust, Huddersfield, UK, 12University Hospital South Manchester, Manchester, UK

09.20-09.40, Hall 1A

Background
Most SCLC patients initially respond to chemotherapy but then relapse and die so new therapies are urgently required. Pre-clinical data shows statins induce growth arrest and apoptosis in SCLC and several other tumour cell types and are additive with chemotherapy. This may in part be due to impaired Ras superfamily function as statins deplete mevalonate, reducing geranylgeranylation and farnesylation of these proteins. We therefore undertook this large pragmatic phase III trial in order to determine if overall survival (OS) was affected by the addition of pravastatin in SCLC

Method
Patients with limited (LD) or extensive (ED) stage SCLC were randomised to pravastatin 40mg OD or placebo for up to 2 years and given standard chemotherapy according to local practice recommended as either cisplatin 60mg/m2 iv or carboplatin AUC 5 or 6 and etoposide 120 mg/m2iv d1 to 3 or 100 mg BD po d2 & 3; max 6 cycles plus radiotherapy as usually given. Patients were excluded if they had used statins within 12 months prior to randomisation. Stratification was: LD vs ED and ECOG 0,1 vs 2,3. Endpoints were: primary - OS; secondary - progression free survival (PFS), local PFS (local control), response rates (RR) and toxicity.

Results
Between 2007 and 2012, 846 patients were randomised, 422 (49.9.%) received pravastatin and 424 (50.1%) placebo in 93 participating sites in the UK. The median age was 64 years (range 54-69); ECOG performance status: 0: 23%; 1: 54%; 2: 17% and 3: 6%; weight 72.6 kg; LD, 357 (42.2%); ED, 479 (56.6%); 211 (24.9%) had ipsilateral effusion and 201 (23.8%) had ipsilateral SCF lymph nodes; Relative Dose intensity of cisplatin/carboplatin and etoposide was 91.6% (range 80.8 to 99.7), and 94.7% (range 85.7 to 100); 83.4% vs 86.3% completed >4 cycles of chemotherapy on the pravastatin and placebo arms respectively. Most patients completed 6 cycles of chemotherapy: 263 (62.3%) vs 265 (62.5%) in the pravastatin vs. placebo groups. Unblinded results showing the effect of pravastatin on OS, PFS, local PFS and toxicity will be presented.

Conclusion
This trial will report on whether pravastatin 40 mg OD added to standard therapy alters the outcome for SCLC patients.
Involved field radiotherapy versus no further treatment in patients with clinical stages IA and IIA Hodgkin lymphoma (HL) and a negative PET scan after 3 cycles ABVD. Results of the UK NCRI RAPID trial

John Radford, Sally Barrington, Nicholas Counsell, Ruth Pettengell, Peter Johnson, Jennie Wimperis, Stewart Coltart, Dominic Culligan, Andrew Lister, Eric Bessell, Anton Kruger, Bilyana Popova, Barry Hancock, Peter Hoskin, Tim Illidge, Mike O’Doherty

1 The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK, 2 PET Imaging Centre, St Thomas’ Hospital, London, UK, 3 Cancer Research UK and UCL Cancer Trials Centre, London, UK, 4 University of Southampton, Southampton, UK, 5 Norfolk and Norwich University NHS Foundation Trust, Norwich, UK, 6 Kent and Canterbury Hospital, Canterbury, UK, 7 Aberdeen Royal Infirmary, Aberdeen, UK, 8 Barts and the London School of Medicine, London, UK, 9 Nottingham City Hospital, Nottingham, UK, 10 Royal Cornwall Hospital, Truro, UK, 11 University of Sheffield, Sheffield, UK, 12 Mount Vernon Cancer Centre, Northwood, UK, 13 St George’s, University of London, London, UK

18.00-18.20, Hall 1A

Background
In the RAPID trial PET response directed therapy was evaluated in early stage HL. Patients (pts) received 3 cycles ABVD followed by a PET scan. If the PET scan was ‘negative’ (score 1 or 2 on 5 point scale) at central review, pts were randomised between IFRT and no further treatment (NFT). If ‘positive’ (score 3, 4 or 5) pts had a 4th cycle ABVD and IFRT. This non-inferiority trial required 400 PET negative pts to be randomised for exclusion of a ≥ 7% difference in 3-year progression-free survival (PFS).

Method
602 pts with previously untreated stages IA/IIA HL and no mediastinal bulk were registered 2003-2010. Following 3 cycles ABVD, 571 pts had a PET scan of which 426 (74.6%) were ‘negative’. 420 PET ‘negative’ pts were randomised to receive IFRT (n=209) or NFT (n=211). 22/209 pts randomised to IFRT did not receive this because 16 pts declined after they became aware of the randomisation decision, 5 had died, 1 had pneumonia.

Results
After median follow-up of 45.7 months, 384/420 (91.4%) PET negative pts are alive/progression-free, 29 (6.9%) are alive/progressed and 7 (1.7%) have died; combined 3-year PFS 92.2% and overall survival (OS) 98.3%. In the IFRT arm, 194 pts are alive/progression-free, 9 have progressed, and 6 have died. In the NFT arm 190 pts are alive/progression-free, 20 have progressed, and 1 has died. 3-year PFS is 93.8% (IFRT) versus 90.7% (NFT) and 3-year OS 97.0% (IFRT) versus 99.5% (NFT). For the 145 PET positive pts, 126 are alive/progression-free, 11 progressed, and 8 died to give a 3-year PFS of 85.9% and OS of 93.9%.

Conclusion
Pts with early stage HL and a negative PET after 3 cycles ABVD have an excellent prognosis without further treatment. This approach reduces treatment time/costs, improves tolerability and removes toxicity of radiotherapy from the PET negative population.

Acknowledgements
The results contained in this abstract were first presented at the American Society of Haematology meeting, Atlanta, GA, December 2012 in the “Best of ASH” category. We are extremely grateful to Leukaemia and Lymphoma Research, the Lymphoma Research Trust and the Department of Health for funding RAPID.
Randomised double-blind phase III trial of cediranib (AZD 2171) in relapsed platinum sensitive ovarian cancer: Results of the ICON6 trial.

Jonathan A Ledermann¹, T Perren², FA Raja¹-², AC Embleton³, GJS Rustin⁴, G Jayson⁵, SB Kaye⁶, A Swart¹-³, M Vaughan⁸, H Hirte⁹

¹Cancer Research UK & UCL Cancer Trials Centre, London, UK, ²St. James University Hospital, Leeds, UK, ³Medical Research Council Clinical Trials Unit at UCL, London, UK, ⁴Mount Vernon Hospital, Northwood, UK, ⁵Christie Hospital, Manchester, UK, ⁶Royal Marsden Hospitals, London, UK, ⁷University of East Anglia, Norwich, UK, ⁸Christchurch Hospital, Christchurch, New Zealand, ⁹Hamilton Regional Cancer Centre, Ontario, Canada

18.20-18.40, Hall 1A

Background
Cediranib is a potent oral inhibitor of VEGFR-1,-2,-3 and inhibits VEGF signalling. A phase III trial in first relapse of ‘platinum-sensitive’ ovarian cancer was performed following evidence of cediranib activity in ovarian cancer and manageable toxicity.

Method
ICON6 is an international three-arm, double-blind placebo-controlled randomised trial. Patients received up to 6 cycles of platinum-based chemotherapy, randomised 2:3:3 to placebo (reference), cediranib 20mg/d during chemotherapy followed by placebo for up to 18 months (concurrent), or cediranib followed by maintenance cediranib (concurrent+maintenance). The primary endpoint was progression-free survival (PFS) in the reference vs. concurrent+maintenance arms. Secondary endpoints were overall survival (OS), toxicity and quality of life.

Results
456 patients from 63 centres were enrolled; median age 62 years, ECOG performance status 0/1. Baseline characteristics, e.g. previous treatment interval >12 months (67%) were balanced between arms. PFS comparing reference and concurrent+maintenance using a log-rank test gave a p-value of 0.00001 with an associated Hazard Ratio (HR) of 0.57 (95% CI 0.45-0.74). However, because of non-proportional hazards (p=0.0237 for PFS and p=0.0042 for OS) the HR can be difficult to interpret, and instead survival time was estimated using restricted means (RM) and HRs are given for completeness. The RM estimates an increased time to progression of 3.2 months from 9.4 to 12.6, during 2 years. Similarly using RM, OS increased by 2.7 months from 17.6 to 20.3 (HR 0.70; log-rank test p=0.0419). PFS using RM for the reference vs. concurrent arms saw an increase of 2.0 months from 9.4 to 11.4 months (HR 0.68; log-rank test p=0.0022). Adverse events significantly more common in the cediranib-maintenance arm were hypertension, diarrhoea, hypothyroidism, hoarseness, haemorrhage, proteinuria and fatigue.

Conclusion
Cediranib given concurrently with platinum-based chemotherapy improves PFS and when continued as maintenance significantly improves both progression-free and overall survival in women with recurrent ovarian cancer.
Symposia

Clinical decision support systems
Room 3A  Hosted by Willie Hamilton, University of Exeter Medical School, UK
11.20 – 11.25  Introduction by the host
11.25 – 11.50  Clinical decision support systems: Some core concepts and questions
Jeremy C Wyatt, Institute of Health Sciences Leeds, UK
11.50 – 12.15  Computer based clinical decision support systems (CDSSs) utilising clinical prediction rules (CPRs) as part of referral for cancer
Tom Fahey, HRB Centre for Primary Care Research, Dublin, Ireland
12.15 – 12.40  Practical implementation of cancer clinical decision support
Willie Hamilton, Peninsula College of Medicine and Dentistry, University of Exeter Medical School, UK
12.40 – 12.50  Discussion

Latest developments in radiotherapy for breast cancer
Hall 1A  Hosted by Alastair M Thompson, Dundee Cancer Centre, UK
11.20 – 11.25  Introduction by the host
11.25 – 11.50  The 2013 George Edelstyn Lecture: The long and the short of radiotherapy fractionation in early breast cancer
John Yarnold, The Institute of Cancer Research, London, UK
11.50 – 12.15  Should all breast radiotherapy be delivered with intensity modulated radiotherapy (IMRT)?
Charlotte Coles, Cambridge University Hospitals NHS Foundation Trust, UK
12.15 – 12.40  How can we reduce cardiac risk for women with left breast cancer?
Anna M Kirby, The Royal Marsden NHS Foundation Trust, London, UK
12.40 – 12.50  Discussion

The bacteriome and cancer
Room 3B  Hosted by Elaine Holmes, Imperial College London, UK
11.20 – 11.25  Introduction by the host
11.25 – 11.50  Diet, the microbiome, and colon cancer risk
Stephen O’Keefe, University of Pittsburgh, USA
11.50 – 12.15  Surgical systems oncology: Translational gut microbiome research in colon cancer
James Kinross, Imperial College London, UK
12.15 – 12.40  Exploring the colorectal cancer microbiome
Julian R Marchesi, Cardiff University, UK
12.40 – 12.50  Discussion

We need to talk about clonal diversity

Room 11  Hosted by Mel Greaves, The Institute of Cancer Research, London, UK

11.20 – 11.25  Introduction by the host

11.25 – 11.50  Phylogenetic quantification of intra-tumour heterogeneity predicts time to relapse in high-grade serous ovarian cancer

Florian Markowetz, Cancer Research UK Cambridge Institute, UK

11.50 – 12.15  Within-tumour diversity as a universal biomarker of prognosis

Trevor Graham, Barts Cancer Institute, London, UK

12.15 – 12.40  Imaging tumour heterogeneity

Robert J Gillies, H Lee Moffitt Cancer Center and Research Institute, Tampa, USA

12.40 – 12.50  Discussion
Clinical decision support systems

Introduction
Willie Hamilton
Peninsula College of Medicine and Dentistry, University of Exeter, UK
11.20 – 11.25, Room 3A
Clinical decision support systems increasingly influence cancer pathways: At the first contact with healthcare (so with a primary care focus), at the level of specialist investigation (mainly in hospital care) and at the level of treatment (the province of oncologists).

Clinical decision support systems: Some core concepts and questions
Jeremy C Wyatt
Institute of Health Sciences, Leeds, UK
11.25 – 11.50, Room 3A
Clinical decision support systems (CDSS) are “active knowledge systems using two or more items of patient data to produce encounter specific advice”1 and have existed since the 1950s. Designing a bias-free RCT of CDSS is challenging1,2 but over 160 RCTS have been carried out. In some settings they are effective3, even when their advice is printed on paper.4 Many different methods can be used to represent the knowledge in CDSS including rules, frames and causal probabilistic networks5, but clinicians are rightly sceptical about neural networks6 whose knowledge base cannot be inspected, as this opens them up to legal liability for damages.7 While CDSS are an attractive way to disseminate evidence based guideline recommendations or help implement tested clinical prediction rules, some key questions are:

1. Against which implementation barriers are CDSS an effective tool?8
2. How to build the CDSS knowledge base for easy maintenance?8
3. How to ensure that the CDSS can access complete patient data in suitably coded form?
4. How to design the advice to maximise its acceptability and impact9 while minimising the known potential for automation bias (professionals unthinkingly following advice even when it is incorrect).10


**Computer based clinical decision support systems (CDSSs) utilising clinical prediction rules (CPRs) as part of referral for cancer**

*Tom Fahy*
HRB Centre for Primary Care Research, Dublin, Ireland
11.50 – 12.15, Room 3A

Clinical prediction rules (CPRs) are clinical tools that quantify the contribution of the history, physical examination and diagnostic tests and then stratify patients according to the probability of having a target disorder. The outcome of interest can be diverse and range across the diagnostic, prognostic and therapeutic spectrum. The most well-known CPR is the Ottawa ankle rule, which distinguishes ankle sprain from ankle fracture. CPRs go through three distinct stages prior to full implementation in a clinical setting: (1) development of the CPR – establishing the independent and combined effect of explanatory variables that can include symptoms, signs or diagnostic tests; (2) narrow and broad validation – where the explanatory variables or clinical predictors in the derivation CPR set are assessed in separate populations; and lastly (3) impact analysis of the CPR – assessed by means of a randomised clinical trial (RCT) where the impact of applying the CPR in a clinical setting is measured either by patient outcome, health professional behaviour, resource use or any combination of these outcomes. We have developed and validated a CPR for women with symptomatic breast complaints. The first part of this presentation will discuss the development and validation of CPRs in relation to the diagnosis and referral of patients with suspected cancer, with reference to breast and colorectal cancer.

We will then discuss the implementation of CPRs as part of computer based clinical decision support systems (CDSSs). CDSSs are information systems designed to improve clinical decision making. They have several critical elements: they are integrated with the electronic patient record; they have a computerised knowledge base; and provide patient-specific information delivered via a software algorithm. The potential for developing and implementing referral guidance for cancer by means of CDSSs will form the second part of this presentation, with critical reference to evidence from randomised trials.

**Practical implementation of cancer clinical decision support**

*Willie Hamilton*
University of Exeter Medical School, UK
12.15 – 12.40, room 3A

The third section of the symposium will describe how clinical prediction rules (CPRs) have been developed in the UK and what progress has been made in practical use of them.

There are two main families of cancer CPRs for primary care use: Risk assessment tools (RATs) and Q-Cancer. They have many similarities, and a few differences. Both families of CPRs have been derived from study of GP records. For RATs, this
was initially from paper records, then from the CPRD, the largest electronic primary care database in the world. RATs used case-control designs, with the outputs being the risk of cancer, expressed as a PPV. These risks were for single symptoms and pairs of symptoms, plus abnormal laboratory results. Q-Cancer used a different large electronic database, and a quasi-prospective design. Read-coded symptoms plus risk factors such as family history are included in a multivariable equation, which can give a PPV as an output.

CPRs have been tested in the UK. Initial testing was of a desk-easel/mousemat design. 614 GPs in 165 English practices used colorectal or lung RATs 2,593 times in 6 months. Compared to the previous six months, there were 292 additional chest X-rays, 104 extra two-week appointments with a chest physician, and 47 more lung cancer diagnoses. For patients with colorectal symptoms, there were 304 more urgent gastroenterological referrals, 270 more colonoscopies and 10 more cancers.

The next phase of development has been to integrate both RATs and Q-cancer into a GP clinical system. This has been done in collaboration between Macmillan and BMJ Informatica, with CR-UK leading the evaluation. A large study is underway in 2013. At the symposium we hope to demonstrate the system live, and to give some early results.

Discussion
12.40 – 12.50

Latest developments in radiotherapy for breast cancer

Introduction
Alastair M Thompson
Dundee Cancer Centre, UK
11.20 – 11.25, Hall 1A

This session will focus on clinical developments in breast cancer radiotherapy. The George Edelstyn Lecture will be delivered by Professor John Yarnold whose international reputation emanates from his rigorous questioning of the principles of breast cancer radiotherapy through hugely influential randomised trials. His focus in this lecture will be on the question of fractionation in which he is a world leader both in breast cancer and in palliative radiotherapy.

The remainder of this session will look at the application of advanced radiotherapy technology to breast cancer. Dr Charlotte Coles will share her thoughts on the role of IMRT to breast radiotherapy. Dr Anna Kirby will then give an update on the technical approaches that attempt to reduce cardiac exposure for women with left sided breast cancer.

The 2013 George Edelstyn Lecture: The long and the short of radiotherapy fractionation in early breast cancer
John Yarnold
The Institute of Cancer Research, London, UK
11.25 – 11.50, Hall 1A

The responses of different normal tissues to daily dose (fraction size) >2.0Gy vary; late-reacting normal tissues being much more sensitive to fraction size than early-reacting normal tissues. Cancers vary too, most types being insensitive to fraction size. All tissues, normal and malignant, are sensitive to total dose. The implication for radiotherapy dose prescriptions is that therapeutic ratio is, on average, optimised by aiming to deliver the highest total dose in the smallest
(≤ 2.0Gy) fractions. Over the last five years, level one evidence confirms that breast cancer is an exception in being as sensitive to fraction size as the dose-limiting late-reacting normal tissues, a conclusion based on 10-year follow up of >8,000 patients entered in randomised clinical trials, including the UK START trials. The result has been to switch from a standard 5-week schedule of 25 fractions to a more convenient 3-week schedule delivering 15 fractions of 2.7Gy. Subgroup analyses based on patient age, breast size, tumour grade, receptor status, node status, surgery, lymphatic radiotherapy and systemic therapies are only fully represented in overviews involving tens of thousands of patients, but those conducted on current data sets are reassuring and suggest that the trial results are generalisable. In patients with left-sided cancer, there is no lower radiation dose threshold for major cardiac events, so the priority is to protect the heart whatever fractionation is used. The brachial plexus is also a critical normal tissue, but whatever estimate of fractionation sensitivity is assumed, 40Gy in 15 fractions delivers a dose intensity lower than 50 Gy in 25 fractions. Current 15-fraction schedules are standard of care for local-regional radiotherapy in the UK, but 15- or 16-fraction regimens are unlikely to represent the lower limit for whole or partial breast external beam radiotherapy. Based on the UK FAST trial testing two 5-fraction schedules of whole breast radiotherapy delivered in five weeks, the current UK FAST Forward trial compares two 5-fraction regimens delivered in one week with a control regimen of 40Gy in 15 fractions. Hypofractionation trials provide an evidence base for the current evaluation of synchronous boost techniques using intensity modulated radiotherapy, approaches that are under evaluation in current UK randomised intensity modulated and partial organ radiotherapy (IMPORT) trials. Over the next five years, the priority is to identify tumour biomarkers predicting fractionation sensitivity that allow patient stratification to larger or smaller fractions. Meanwhile, a 5-fraction regimen of local-regional radiotherapy for women with early breast cancer is a realisable research outcome by the end of this decade.

Should all breast radiotherapy be delivered with intensity modulated radiotherapy (IMRT)?
Charlotte Coles
Cambridge University Hospitals NHS Foundation Trust, UK
11.50 – 12.15, Hall 1A

This presentation will describe the rationale, indications and evidence for breast intensity modulated radiotherapy (IMRT) and outline different methods of delivery. Simple forward-planned IMRT can improve dose homogeneity to the whole and partial breast in cases where dose exceeds ICRU recommendations. More complex IMRT can be used in situations where a steep dose gradient is required, for example to deliver good coverage to the breast and acceptable dose to organs at risk when this cannot be achieved with tangents. It can also be used to deliver a simultaneous integrated boost and hence reduce the total number of treatment fractions.

There is phase III trial evidence showing clinical benefit for use of IMRT to improve dose homogeneity across the breast. Randomised trials are currently open which will evaluate the role of IMRT for simultaneous integrated boost compared with whole breast radiotherapy and sequential boost. The evidence for both these indications will be presented.

The various methods of breast IMRT will be outlined. More complex IMRT can produce a low dose ‘bath’ to normal tissue. The long term effect of this is unknown. Therefore the majority of patients should receive predominantly tangent based treatments as this is an effective method of minimising dose to adjacent organs at risk, such as the heart and lungs.

In summary, breast IMRT can vary from simple to very complex methods. It is likely that the vast majority of patients with breast cancer will benefit from some form of IMRT and all should have the opportunity to access this technology if indicated.
How can we reduce cardiac risk for women with left breast cancer?
Anna M Kirby
The Royal Marsden NHS Foundation Trust, London, UK
12.15 – 12.40, Hall 1A

Adjuvant breast radiotherapy improves local control and survival from breast cancer but, despite improvements in techniques over the last few decades, remains associated with an increased risk of death from cardiac disease, particularly ischaemic heart disease. Recent data suggest that the risk of major coronary events increases by 7.4% per 1Gy increase in mean heart dose, and that there is no threshold below which the risk of late cardiac effects is zero. Where the balance of benefits versus risks is in favour of radiotherapy, we should therefore aim to keep mean heart doses from adjuvant breast and/or locoregional radiotherapy as low as reasonably practicable.

A number of heart-sparing breast radiotherapy techniques can be employed, including optimisation of beam angles, use of cardiac shielding using multileaf collimation, intensity modulated radiotherapy, prone positioning and deep-inspiratory breath-hold (DIBH) techniques. The UK HeartSpare study IA compared active-breathing controlled_DIBH (ABC_DIBH) with a cheaper and simpler voluntary_DIBH (v_DIBH) technique. The latter was found to be as reproducible as ABC_DIBH, and the two techniques achieved comparable heart-sparing. V_DIBH is now being compared with prone positioning in larger breasted-women, whilst the feasibility of its implementation nationally is being tested in a multicentre study involving five UK centres. Strategies for increasing availability of heart-sparing radiotherapy beyond the HeartSpare study will be discussed in the context of improving outcomes for women undergoing left breast radiotherapy nationally.

Discussion
12.40 – 12.50

The bacteriome and cancer

Introduction
Elaine Holmes
Imperial College London, UK
11.20 – 11.25, Room 3B

The recent recognition of the symbiotic gut microbiome (which is now estimated to have over 10 million genes) as a fundamental component of human biology has led to an explosion of interest in microbial variation in relation to the pathogenesis of non-infectious diseases, including cancers and variation in individual responses to therapy. There is growing evidence that microbiome activities are relevant to many areas of cancer research from basic mechanisms to improving and personalising treatments. This session presents three exemplar views of the microbiome universe – from the perspectives of basic microbiotal compositional and function, a cancer aetiopathogenesis and from the perspective of cancer therapy and surgery.

Diet, the microbiome, and colon cancer risk
Stephen O’Keefe
University of Pittsburgh, USA
11.25 – 11.50, Room 3B

Geographical and migration epidemiological studies, backed up by experimental studies, have produced overwhelming
evidence that diet drives colon cancer risk, with high intakes of meat and fat increasing risk, and high consumption rates of fibre rich foods, such as grains, fruits and vegetables, reducing risk. To test our hypothesis that cancer risk is determined by the effect the diet has on the composition and function of the microbiota to produce metabolites that either promote mucosal health or are inflammatory and neoplastic, we have conducted studies in populations of high and low risk, namely African Americans who have the highest risk in the USA, and rural Africans, who rarely get the disease, and confirmed that high meat and fat intakes in Americans were associated with increased mucosal proliferation rates – a biomarker of cancer risk, while high fibre African diets were associated with low proliferation rates. Simultaneous measurement of the microbiota and metabolome showed dramatic differences in the microbiota composition and function. The structure of the African colonic microbiota was considerably more robust, with amplification of the bacterial groups associated with complex plant carbohydrate degradation and butyrate production. Targeted analysis confirmed higher numbers of butyrate-producing bacteria and butyrate, which has profound anti-neoplastic properties in experimental models. In contrast, secondary bile acid producing bacteria and their products, which have carcinogenic properties, were higher in African Americans. Most recently, we have demonstrated that dietary switch between these two populations produces reciprocal changes in the microbiome, metabolome, and mucosal biomarkers of risk within 2 weeks, leading to the conclusion that modification of the diets of westernized populations to contain high fibre (>45g/d) foods, such as grains and beans, together with lower intakes of animal fats, can be expected to have an immediate effect on cancer risk.

Surgical systems oncology: Translational gut microbiome research in colon cancer
James Kinross
Imperial College London, UK
11.50 – 12.15, Room 3B

The Imperial College Clinical Phenome Centre (CPC) deploys nuclear magnetic resonance (NMR) and mass spectrometry (MS) based platforms for near real time mapping of the surgical patient journey. This systems medicine approach is being used to explore the biochemical and functional impact of the gut microbiome on colon cancer biology. This is because the dietary-microbiome axis is essential to the initiation of colon cancer, and the microbiota directly influence the toxicity and efficacy of both surgical and medical therapeutic interventions. The CPC is therefore developing novel diagnostic technologies that account for the gut cancer microbiome and which function in the near real time scale for intra-operative use and for use in the critical care setting. This talk will therefore provide an overview of how surgical systems medicine is providing novel insights into the importance of the gut microbiome in colon cancer and outline why host-microbiome interactions are essential for the development of next generation ‘precision’-based surgical oncological therapies.

Exploring the colorectal cancer microbiome
Julian R Marchesi
Cardiff University, UK
12.15 – 12.40, Room 3B

The human microbiome has been implicated in a wide range of host diseases, such as heart disease, inflammatory bowel disease, diabetes and metabolic syndrome. In the last decade its role in colorectal cancer (CRC) has started to attract more interest. Since CRC is increasingly seen as a disease which is driven by environmental rather than genetic factors, the gut microbiome has been investigated as a potential driver of this disease. This talk will describe how multi-modal ‘omic’ technologies are being used to investigate the interaction of the gut microbiome with this disease and explore
Symposia abstracts

how some microbes are being exploited as therapeutic agents.

Discussion
12.40 – 12.50

We need to talk about clonal diversity

Introduction
Mel Greaves
The Institute of Cancer Research, London, UK
11.20 – 11.25, Room 11

Intraclonal genetic diversity in individual patients’ cancer cells is predictive of drug resistance and poor outcome. A major challenge of cancer therapeutics is how to thwart the resilience of the evolutionary process. This session will address three key aspects of this topic:

• How we can best measure diversity?
• Does the degree of diversity predict outcome?
• How can we tackle or bypass clonal diversity, therapeutically?

Phylogenetic quantification of intra-tumour heterogeneity predicts time to relapse in high-grade serous ovarian cancer
Florian Markowetz
Cancer Research UK Cambridge Institute, UK
11.25 – 11.50, Room 11

Intra-tumour genetic heterogeneity is the result of ongoing evolutionary change within each cancer. The expansion of genetically distinct sub-clonal populations may explain the emergence of drug resistance and if so would have prognostic and predictive utility. However, methods for objectively quantifying tumour heterogeneity have been missing and are particularly difficult to establish in cancers where predominant copy number variation prevents accurate phylogenetic reconstruction because of horizontal dependencies caused by long and cascading genomic rearrangements.

To address these challenges we have developed MEDICC, a method for phylogenetic reconstruction and heterogeneity quantification, which determines optimal phasing of major and minor alleles, computes evolutionary distances between samples, and reconstructs ancestral genomes. Rigorous simulations and an extensive clinical study show the power of our method, which outperforms state-of-the-art competitors in reconstruction accuracy and additionally allows unbiased numerical quantification of tumour heterogeneity.

Using MEDICC we investigated the relationship between tumour heterogeneity and patient outcome in high-grade serous ovarian cancer. We found that tumour heterogeneity in this cancer is driven by ongoing clonal evolution with fully branched evolutionary trajectories that do not have clock-like evolutionary rates. Quantitative measures of clonal expansion and temporal heterogeneity were the strongest predictors of progression-free survival. We show in 2 patients that clonal expansion of a minor subclone that was present prior to chemotherapy led to clinical relapse.
Within-tumour diversity as a universal biomarker of prognosis
Trevor Graham
Barts Cancer Institute, London, UK
11.50 – 12.15, Room 11

Carcinogenesis is fundamentally an evolutionary process; establishing the prognosis for a cancer therefore requires predicting the future course of tumour evolution. The same is true in premalignant conditions: The risk of developing cancer is determined by how the premalignant lesion is evolving.

The level of diversity within a population largely determines how fast that population will evolve. If there is no diversity natural selection cannot operate, whereas diverse populations are likely to contain well-adapted individuals that can prosper in changing environments. Consequently, quantification of within-tumour diversity is likely to be a proxy-measure of the rate of the underlying evolutionary process that drives carcinogenesis.

In this talk, I will describe how we have measured within-tumour diversity, both genetically and phenotypically, and used these measures to successfully determine prognosis in both established cancers and in premalignant lesions. I will focus particularly on lung cancer and the premalignant condition Barrett’s Oesophagus. Building upon this work, I will present the case for the quantification of within-tumour diversity as a universal biomarker for cancer prognosis.

Imaging tumour heterogeneity
Robert J Gillies
H. Lee Moffitt Cancer Center and Research Institute, Tampa, USA
12.15 – 12.40, Room 11

It is becoming increasingly appreciated that malignant cancers can be characterised by genetic plasticity within highly selective local microenvironments. This combination promotes somatic evolution and the emergences of clades of cells in spatially explicit micro-habitats. Malignancy can be defined by these habitats, which increase the probability that cancers will develop therapy resistant phenotypes. Heterogeneity across cancers has been known at the nuclear level for years and is recognised as a strong predictor of poor prognosis. For most advanced cancers and most patients, response to therapy is fleeting, owing to the inevitable evolution and proliferation of a resistant population.

Induction of genomic alterations and localised selection by heritable and/or environmental factors will result in phenotypic heterogeneity. Phenotypic and physiologic heterogeneity can be viewed radiographically, wherein non-uniform patterns of enhancement or attenuation can be associated with poor outcome. In order to systematically address this issue, we have created a database structure that can be populated with images, as well as quantitative image feature data that can be mined in combination with patient outcomes and genetic data from biopsies. This enterprise is termed ‘Radiomics’, which allows real-time data analyses and association of features with prognostic, diagnostic and predictive models. The goal of radiomics is to convert images to mineable data, with high fidelity and high throughput. The radiomics enterprise can be divided into a pipeline of processes with definable inputs and outputs, each with its own challenges that need to be overcome. Each of these steps must be developed de novo and, as such, poses discrete challenges that have to be met. Even though this field is in its infancy, meaningful classifier models have been generated in detecting and diagnosing a number of cancer subtypes.

To date, the radiomics effort has focused on agnostic and semantic image features, which quantify indescribable and describable features, respectively. An example of an agnostic feature is image ‘entropy’, determined by the randomness of pixel intensities in a near-neighbourhood. Examples of a semantic feature are ‘spiculated’, ‘spherical’, ‘central necrosis’
which are commonly used as descriptors for tumour anatomy. These have all been shown to have high prognostic value in non-small cell lung cancer (NSCLC) and are being used to classify indeterminate lung nodules in lung screening CTs. More recently, we have been combining orthogonal MR images (e.g. STIR, Diffusion and Contrast enhanced T1) to develop data cubes for each voxel, which can then be clustered using fuzzy logic to identify specific sub-tumoural ‘habitats’; each with their own unique combination of perfusion, lipid/water ratio and cellular density. We hypothesise that these habitats describe specific sub-tumoural regions associated with genetic clades, and hence may inform the application of targeted therapy.

Thank you to Olya Grove and Robert A Gatenby (H. Lee Moffitt Cancer Center and Research Institute, Tampa, USA) who also contributed to this work.

Discussion
12.40 – 12.50
BACR educational workshop: Relative merits of ctDNA and CTCs as circulating biomarkers to aid cancer patient management

Hosted by Jacqui Shaw¹, Caroline Dive², Ged Brady² and Nitzan Rosenfeld³
1University of Leicester, Leicester, UK, ²Cancer Research UK Manchester Institute, UK, ³Cancer Research UK Cambridge Institute, UK

08.00 – 08.45, Room 11

Circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA), the tumour derived component of circulating free DNA (cfDNA), are under active investigation in translational cancer research. High CTC counts generally indicate poor prognosis and in the metastatic setting a fall in CTC counts while on treatment may mean a patient will live longer. ctDNA is also a rapidly growing area, particularly in monitoring response to therapy. Important recent advances in next generation sequencing have demonstrated multiple mutations in parallel in the same sample, providing information on tumour evolution. Therefore, both CTCs and ctDNA have potential as a ‘liquid biopsy’ to identify genomic changes in a cancer and to monitor cancer patients over time by blood tests. Some of the key questions under current active scrutiny include:

• Do CTCs/ctDNA reflect tumour biology in the primary/metastases?
• Can CTCs/cfDNA detect minimal residual disease following tumour resection and can dynamic changes predict recurrence?
• How is intratumour heterogeneity manifested in CTCs/ctDNA at recurrence?
• Do CTCs/ctDNA have utility in cancer screening?

This session will contrast the relative merits of CTCs and ctDNA and provide a brief insight into current active areas of research. Short presentations will be given by scientists focusing on CTCs and ctDNA, describing their current activities and perspectives.

This is a great opportunity to gain up to the minute information on this rapidly evolving field and to ask questions of the experts in an interactive session.

Charles Rivers workshop: Cutting edge cancer modelling using the NSG mouse

Hosted by Charles Rivers UK Ltd and The Jackson Laboratory

08.00 – 09.00, Room 4

The highly immunodeficient NOD scid gamma (NSG) mouse strain enables innovative cancer research modeling that was previously impossible. This seminar will explain how NSG mice increase the efficiency, sophistication and personalisation of modeling oncology, including applications with cancer stem cells, patient-derived xenografts and challenging blood tumours.

Dr Kathy Snow, The Jackson Laboratory
**Commercial workshop: Headlines of International Congresses in 2013**

**Sponsored by Roche Products Limited**

**Hosted by Mark Verrill¹ and Karen Verrill²**

¹Northern Institute for Cancer Research, Newcastle General Hospital, UK and ²Maggie’s Newcastle, Freeman Hospital, UK

13.00 – 14.00, Room 11

The latest developments in cancer research and treatment are presented first at conferences across the world; the largest and most prestigious outside of the UK is the American Society of Clinical Oncology. However, downward pressure on study leave and sponsorship budgets increasingly limits opportunities for UK delegates to attend. This symposium will showcase the key data across the spectrum of cancer from ASCO and other key conferences in the last year, giving an independent view and reviewing the data in a UK context.

This symposium is sponsored by Roche Products Limited – with no editorial control on content.

*Lunch will be provided in the room*

**Improving the design and reporting of studies on early diagnosis across all cancer types**

**Hosted by Richard Neal, Bangor University, Wrexham, UK**

14.30 – 16.00, Room 3B

It has been recognised that in early diagnosis research, huge differences exist in the definitions of different time points and intervals, as well as suboptimal methods and reporting. Published in 2012 in BJC, the Aarhus Consensus Statement aims to improve the design and reporting of studies on early cancer diagnosis. It defines time periods and intervals and includes a checklist for future studies. The speakers will introduce the statement and then open the discussion.

This workshop arises from NCRI Screening Prevention and Early Diagnosis (SPED) group.

**“What I’d like to talk to you about now is a clinical trial...”**

**Hosted by Alison Ames and Chris Hough, Northern Networks Facilitator Group, UK**

14.30 – 16.00, Room 4

This can be a difficult concept to approach with a patient, but there are skills we can all acquire to make this type of conversation easier.

This 90-minute taster session will cover elements of four interactive modules, based on the Fallowfield and Jenkins evidence based programme, to improve how information about randomised controlled trials is communicated to potential trial participants.

The primary content is facilitator-led group discussion around phase III trials depicted in DVDs of real doctors and nurses and simulated patients.
This is an excellent training opportunity for specialist nurses, doctors and other healthcare professionals who come into contact with trial participants, to develop their knowledge and skills.
Cancer awareness and population studies

	

Hall 1B

Hosted by Jane Wardle, University College London, UK

14.30 – 14.40

HPV prevalence in screened population and types associated with cervix disease in Northern Ireland

Lesley Anderson, Queen’s University Belfast, UK

14.40 – 14.50

The effectiveness of a brief telephone-based intervention to improve fatigue in prostate cancer: A feasibility study

Ben Langston, King’s College London, and Prostate Cancer UK, London, UK

14.50 – 15.00

Mismatch between cancer symptom knowledge and symptom attribution in daily life: A population-based study

Katriina Whitaker, University College London, UK

15.00 – 15.10

Recognition of cancer warning signs and anticipated time to help-seeking in a population sample of adults in the UK

Samantha L Quaife, University College London, UK

15.10 – 15.20

The effect of repeated invitations to prevalence screening on inequalities in the NHS Bowel Cancer Screening Programme

Christian von Wagner, University College London, UK

15.20 – 15.30

Age, smoking status and socioeconomic status as predictors of participation in the UK Lung Screen (UKLS) randomised controlled trial of low dose computed tomography (LDCT) for the early detection of lung cancer

Fiona McRonald, The University of Liverpool, UK

15.30 – 15.40

Cancer in patients with mental illness - differences and outcomes

Anna Gavin, Queen’s University Belfast, Belfast, UK

15.40 – 16.00

Discussion

The cancer cell and model systems II

Room 11

Hosted by Julian Downward, Cancer Research UK London Research Institute, UK

14.30 – 14.40

The c-MET-JAK1/2-STAT3 signalling axis is regulated by ADAM17 and is a key mediator of resistance to MEK inhibition in KRAS mutant colorectal cancer

Sandra Van Schaeybroeck, Queen’s University Belfast, UK

14.40 – 14.50

Measurement of the acute response to hypoxia in rat tumours in vivo using magnetic resonance spectroscopy and hyperpolarised pyruvate

Joanne Bluff, University of Sheffield, UK

14.50 – 15.00

PTEN phosphatase-independent maintenance of apical membrane integrity during colorectal glandular morphogenesis

Ravi Deevi, Queen’s University of Belfast, UK
### Proffered paper sessions

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<tr>
<th>Time</th>
<th>Title</th>
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<td>15.00 – 15.10</td>
<td>Parallel functional genetic and compound screens identify WEE1 inhibition as a therapeutic strategy for cancers with defects in Fanconi Anaemia and HR pathways</td>
<td>Marieke Aarts</td>
<td>Breakthrough Breast Cancer Research Centre, The Institute of Cancer Research, London, UK</td>
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<tr>
<td>15.10 – 15.20</td>
<td>The role of JAK1/2-STAT3 as acute resistance mechanism to MEK inhibition in BRAF mutant colorectal cancer cell lines</td>
<td>Basak Celtikci</td>
<td>Queen’s University Belfast, UK</td>
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### Diagnosis and therapy

Room 3A

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Proffered paper sessions

15.35 – 15.45 Preliminary results of the GALA-5 study: an evaluation of the tolerability and feasibility of combining 5-Amino-Levulinic Acid (5-ALA) with carmustine wafers (Gliadel) in the surgical management of primary glioblastoma
Colin Watts, University of Cambridge, UK

15.45 – 16.00 Discussion

Radiotherapy and radiobiology

14.30 – 14.40 Simultaneous cone beam CT scanning during prostate radiotherapy produces clinically useful images
Chris Boylan, The Christie NHS Foundation Trust, Manchester, UK

14.40 – 14.50 FDG-PET parameters as predictors for outcome in non small cell lung cancer (NSCLC) treated with stereotactic body radiotherapy (SBRT)
Katy Clarke, St James’s University Hospital, Leeds, UK

14.50 – 15.00 Does the incidental coverage of axillary nodes by either standard breast or high tangential radiotherapy fields explain Z0011 trial results?
Marjory Maclennan, Edinburgh Cancer Centre, UK

15.00 – 15.10 A significant reduction in positive circumferential margin involvement is achieved by combining a low rectal cancer MRI staging system with clinical assessment and sound patient management: experience from the MERCURY II Low Rectal Cancer Study
Nick Battersby, Pelican Cancer Foundation, Basingstoke, UK

15.10 – 15.20 Increased blood flow to human rectal cancer induced by nelfinavir and radiotherapy
Esme Hill, University of Oxford and Churchill Hospital, Oxford, UK

15.20 – 15.30 An evidence-based UK IMRT solution for anal cancer: the development of the control arm for future UK led clinical trials
Rebecca Muirhead, Gray Institute for Radiation Oncology & Biology, Oxford, UK

15.30 – 15.40 Preoperative chemoradiation (CRT) with concurrent cetuximab, irinotecan and capecitabine in MRI-defined locally advanced rectal cancer (LARC) within the phase II EXCITE trial: Relationship of epidermal growth factor receptor (EGFR) pathway mutations to histological response and survival
Simon Gollins, North Wales Cancer Treatment Centre, Denbighshire, UK
15.40 – 16.00 Discussion
Cancer awareness and population studies

Hosted by Jane Wardle, University College London, UK

HPV prevalence in screened population and types associated with cervix disease in N. Ireland
Lesley Anderson¹, Michael O’Rorke², Robbie Wilson³, Jackie Jamison⁴, Anna Gavin⁵
¹Centre for Public Health, Queen’s University Belfast, Belfast, UK, ²Centre for Public Health, Queen’s University Belfast, Belfast, UK, ³Northern Health and Social Care Trust, Antrim Area Hospital, Antrim, UK, ⁴Northern Health and Social Care Trust, Antrim Area Hospital, Antrim, UK, ⁵N. Ireland Cancer Registry, Queen’s University Belfast, Belfast, UK
14.30 – 14.40, Hall 1B

Background
With the introduction of HPV vaccination, the profile of HPV in the community is expected to change. This study aimed to determine the prevalence of HPV infection among screening age women prior to vaccination and determine HPV types associated with cervix disease.

Method
HPV positivity was investigated using the Roche Cobas 4800 in 5557 eligible Liquid Based Cytology (LBC) samples from women of screening age in Northern Ireland and 2048 samples of cervical pathology collected prospectively.

Results
LBC samples revealed a crude age standardised prevalence of high risk HPV of 17.4% in screening age women in Northern Ireland. The highest rate (42.5%) was in those aged 20-24. HPV prevalence by main subtypes were: HPV 16 (5.3%) 31 (2.5%) 51 (2.2%) 18 (1.7%). For cervical pathology prevalence of HPV was 64.7% overall, increasing from 48.1% of CINI, 65.7% of CINII, 81.3% of CINIII to 89.1% of cervical squamous cell carcinomas (SCC). The majority of SCC’s tested positive for HPV16 or 18 (91.2% of HPV positive samples). HPV positivity was found in 92.9% microinvasive SCC, 50% of adenocarcinomas, 66.7% adenosquamous carcinomas, 88.2% cervical glandular intraepithelial neoplasia and 29.1% koilocytosis. The number of genotypes detected varied across pathology grade. On average 2.5 genotypes where detected per positive sample. A trend was identified that CIN I had the lowest percentage (66.0%) of single genotypes. On average 91.8% of all cancerous samples containing only one HPV genotype. The most frequent single genotypes found in cancerous samples were HPV16, HPV18, HPV45, HPV31, HPV39 and HPV52.

Conclusion
For SCC samples not testing positive for HPV16 or HPV 18, five samples tested positive for a single HPV 31, HPV 39, HPV 45 or HPV 52 genotype, which may have implications for vaccine cross protection of non-target genotypes as these types are common in women with normal cervical pathology.

Acknowledgements
The N. Ireland Cancer Registry is funded by the Public Health Agency, Northern Ireland. Thanks to the R & D Office, Public Health Agency and Department of Health, Social Services and Public Safety, Northern Ireland who funded this work.
The effectiveness of a brief telephone-based intervention to improve fatigue in prostate cancer: A feasibility study

Ben Langston1,2, Jo Armes1, Lucy Elliott2, Jocelyne James2, Emma Ream1
1King’s College London, London, UK, 2Prostate Cancer UK, London, UK
14.40 – 14.50, Hall 1B

Background
Cancer-related fatigue is a significant clinical symptom commonly experienced by men during and following treatment for prostate cancer. It is distressing, interferes with functioning, and is often under-acknowledged by healthcare professionals. The study aimed to evaluate the effectiveness of a brief telephone-based intervention for fatigue delivered by Specialist Nurses at Prostate Cancer UK.

Method
A randomised control trial design was adopted. Men experiencing fatigue during or following treatment for prostate cancer were eligible to participate and were randomly allocated between waiting list control group receiving usual care or the intervention. The intervention comprised psychological support, self-care education and goal setting for behaviour change. It was delivered using motivational interviewing via 4 telephone calls over 10 weeks. Outcomes were assessed at baseline and at trial completion using the BFI, FDS, HADS, NRS (fatigue management) and EORTC-QLQ-C30. Analysis consisted of Mann-Whitney Tests for between group comparisons.

Results
76 men were recruited. Fatigue in study groups was equivalent at baseline. Post-trial between group analysis showed the intervention group reported improved global fatigue (p=.005), fatigue severity (p=.001), fatigue management (coping with fatigue in daily life) (p=.031), social functioning (p=.028) and fatigue symptoms (p=.018).

Conclusion
The findings show the effectiveness of brief a telephone intervention at improving fatigue, fatigue management and social functioning. This represents a sustainable model of intervention delivery which is acceptable to men with prostate cancer and is effective in producing positive outcomes.

Acknowledgements
Professor Emma Ream and Dr Jo Armes at King’s College London for their support in the development of the intervention and the research. Patricia Smith, Teresa Lynch, John Robertson, Lucy Elliott and Jocelyne James from Prostate Cancer UK for support in trial delivery. The men who took part our research.

References
Mismatch between cancer symptom knowledge and symptom attribution in daily life: A population-based study
Katriina Whitaker1, Una Macleod1, Alice Simon4, Suzanne Scott2, Jane Wardle1
1University College London, London, UK, 2King’s College London, London, UK, 3Hull York Medical School, Hull, UK, 4City University, London, UK
14.50 – 15.00, Hall 1B

Background
Failure to recognise symptom seriousness is a common reason given for delay in cancer presentation. However, recent studies have demonstrated that the public has good knowledge of warning signs for cancer; indicating that delay cannot be due to lack of knowledge per se. We collected symptom data in a population-based sample to investigate whether formal knowledge that a symptom is a ‘warning sign’ for cancer was related to making a cancer attribution when the symptom was experienced.

Method
A postal survey was sent to 4931 adults (>50 years, no cancer diagnosis), from 3 General Practices in England, asking about recent experience (past 3 months) of 17 symptoms, including 10 ‘cancer warning signs’ symptoms. The survey was presented as a health survey to avoid cancer focus. Follow-up questions asked about perceived cause and perceived seriousness for each reported symptom. Knowledge of warning signs was assessed with items from the CAM1, embedded among questions about other illnesses.

Results
Over half the respondents (915/1724: 53%) reported at least one ‘cancer warning sign’ symptom. However, only 23 (1.3%) spontaneously mentioned cancer as a possible cause. A higher proportion (40%) thought the symptom might be serious, ranging from 28% (18/64) of respondents with unexplained weight loss to 62% (154/247) for unexplained pain. Multiple regression analyses on a symptom-by-symptom basis showed that ‘knowledge’ of that item on the CAM did not predict a cancer attribution or perceived seriousness, except for unexplained bleeding where knowledge was associated with higher perceived seriousness (beta=0.25, p<.05).

Conclusion
When asked about ‘real-time’ symptom experience, theoretical knowledge of cancer warning signs did not translate to making a cancer attribution, or to higher perceived seriousness. Further work is needed to understand why cancer schema are not activated when people engage in symptom appraisal.

Acknowledgements
Thank you to the participants who took part in the survey, Cancer Research UK for funding the research and Dr Kelly Winstanley for her helpful comments.

References
Recognition of cancer warning signs and anticipated time to help-seeking in a population sample of adults in the UK

Samantha L Quaife¹, Lindsay JL Forbes², Amanda J Ramirez³, Kate E Brain³, Conan Donnelly⁴, Alice E Simon⁵, Jane Wardle¹

¹Health Behaviour Research Centre, University College London, London, UK, ²Promoting Early Presentation Group, King’s College London, London, UK, ³Cochrane Institute of Primary Care and Public Health, Cardiff University, Cardiff, UK, ⁴Centre for Public Health, Queen’s University Belfast, Belfast, UK, ⁵City University, London, UK

15.00 – 15.10, Hall 1B

Background
Lack of recognition of cancer warning signs is implicated in delay in help-seeking in retrospective reports from cancer patients. In one population-based study, an aggregated recognition score was associated with anticipating a longer average help-seeking delay for potential cancer symptoms. The present analysis tested the hypothesis that anticipated delay for individual symptoms would be longer in those who did not recognise the relevant warning sign.

Method
A population-based sample of 6965 UK adults (age >50 years) completed telephone interviews using the validated Awareness and Beliefs about Cancer scale,¹ which assesses anticipated help-seeking for potential cancer symptoms, recognition of warning signs, demographics, and healthcare access. Symptoms used in this analysis were breast changes, rectal bleeding and persistent cough; asking how long the respondent would wait before making a doctor’s appointment. We used >2 weeks as the cut-off to match the previous study,² but also did sensitivity analyses with alternative durations. The related warning signs were unexplained lump, unexplained bleeding and persistent cough; asking whether each one could be a warning sign for cancer (yes/no).

Results
For each symptom, more respondents who did not recognise the related warning sign anticipated >2 weeks delay: 17% vs 8% for breast changes, 11% vs 7% for rectal bleeding, 53% vs 49% for persistent cough. Multivariable logistic regression showed significant effects of recognition for delay for breast changes (OR=2.45, 95% CI 1.47-4.08), rectal bleeding (OR=1.77, 1.36-2.30), and persistent cough (OR=1.30, 1.17-1.46), independent of age, sex, education, ethnicity, and healthcare access. Effects were the same using a 4 week cut-off.

Conclusion
Lack of recognition that a symptom could be a warning sign for cancer was associated with anticipating greater delay in help-seeking. Future studies should use behavioural rather than anticipated outcomes to estimate the contribution of awareness of warning signs to patient delay in diagnosis.

Acknowledgements
The Policy Research Unit in Cancer Awareness, Screening and Early Diagnosis receives funding for this research programme from the Department of Health Policy Research Programme. The views expressed are those of the authors and not necessarily those of the NHS or the Department of Health.

References

The effect of repeated invitations to prevalence screening on inequalities in the NHS Bowel Cancer Screening Programme

Siu Hing Lo1, Christian von Wagner2, Julia Snowball2, Stephen Halloran2,3, Jane Wardle1

1University College London, London, UK, 2Bowel Cancer Screening Programme, Southern Hub, Royal Surrey County Hospital, Surrey, UK, 3University of Surrey, Surrey, UK

15.10 – 15.20, Hall 1B

Background
The NHS Bowel Cancer Screening Programme (BCSP) invites all age-eligible adults for colorectal cancer screening using a Faecal Occult Blood (FOB) test every two years, irrespective of previous uptake. Existing research has shown that repeated invitations engage some previous non-responders, but it is unknown what effect continued offers of screening have on socioeconomic and gender inequalities in uptake and clinical outcomes.

Method
Data from the Southern BCSP Hub of all individuals (n= 62,099) aged 60-64 years at the time of first invitation to prevalence screening (September 2006 - February 2008) with a follow-up period of at least 4 years and 9 months were analysed. Of the 62,099, 23,677 received a second and 16,656 also received a third invitation to prevalence screening. The dataset included information on invitation dates, return dates if the FOB test had been completed, FOB positivity, colonoscopy or other follow-up test uptake, diagnostic outcomes, gender, age and an area-level measure of socioeconomic deprivation (IMD score).

Results
Uptake was 57% for the first, 23% for the second and 15% for the third invitation to prevalence screening, resulting in a cumulative uptake of 70%. Women were more likely to accept the first (OR= 1.39, 95% CI: 1.34-1.43) and second (OR= 1.09, 95% CI: 1.02-1.15) invitation, but less likely to accept the third invitation to prevalence screening (OR= 0.88, 95% CI: 0.81-0.96). More deprived invitees were less likely to accept any of the invitations to prevalence screening (results for IMD quintiles: 1st invitation: OR= 0.87, 95% CI: 0.86-0.88; 2nd: OR= 0.88, 95% CI: 0.86-0.90; 3rd: OR= 0.89, 95% CI: 0.86-0.92). Overall colonoscopy or other follow-up test attendance was very high, with few differences between socio-demographic groups.

FOB positivity rates were higher among individuals screened following their second (2.6%, p<.001) or third invitation (3.3%, p<.001) than for those screened following their first invitation (1.2%). Overall, cancer and adenoma detection rates were also higher among individuals screened after multiple prevalence screening invitations (result patterns differ per diagnostic outcome).

Conclusion
Repeat invitations are effective at increasing prevalence screening. They also reduce gender inequality, but the socioeconomic gradient remains stable across multiple invitation rounds for prevalence screening. Abnormal diagnostic outcomes are more common among individuals who delay prevalence screening.

Age, smoking status and socioeconomic status as predictors of participation in the UK Lung Screen (UKLS) randomised controlled trial of low dose computed tomography (LDCT) for the early detection of lung cancer

Fiona McRonald1, David Baldwin2, Anand Devaraj3, Kate Brain4, Tim Eisen5, John Holemans6, Martin Ledson6, Nicholas Screaton7, Robert C Rintoul5, Ghaseem Yadegarfar1, Kate Lifford4, David Whynes3, Keith Kerr4, Richard Page6, Mahesh Parmar9, David Weller10, Paula Williamson11, David M Hansell11, Stephen W Duffy12, John K Field1
Background
Lung Cancer causes over 35,000 UK deaths per year: early detection by CT screening has been shown to reduce mortality in the USA.

Method
UKLS is a pilot RCT, utilising LDCT screening of individuals at high lung cancer risk (>5% over 5yrs). UKLS is population-based, approaching people of 50-75yrs through local PCT records, and using a validated lung cancer risk prediction model to identify high risk individuals from the target group. We report observations made from the initial recruitment to the trial.

Results
Of 88,897 individuals approached in Liverpool and Cambridgeshire, 26.8% responded positively to the first questionnaire. People aged 50-55yr were least likely to respond, and at lowest lung cancer risk: only five of 26,532 (0.02%) attended clinic. Response rate increased with socioeconomic status (SES), varying from 19.6% in the lowest Index of Multiple Deprivation (IMD) quintile to 34.2% in the highest quintile. However, this was offset by the higher lung cancer risk in more deprived socioeconomic groups, hence a representative proportion of the high risk positive responders (i.e. those included in the RCT) were from the lowest IMD quintile. Calculations based on age-adjusted population smoking figures suggested that ex-smokers were the most responsive to the study invitation, and current smokers the least responsive. This trend was apparent across all IMD quintiles, and was not merely due to confounding.

Conclusion
We have identified high risk individuals in relatively equal proportions across all IMD quintiles, demonstrated that very few people aged 50-55yr are at high risk, and shown that current smokers are least likely to participate in screening. These observations may have implications for cost effectiveness; consideration needs to be given to inclusion criteria for any future UK screening trial. Substantial investment is required for an awareness campaign to coincide with any future national lung cancer CT screening programme.

Cancer in patients with mental illness - differences and outcomes
Anna Gavin, Suzanne Cromie, David Donnelly
Queen’s University Belfast, Belfast, UK
15.30 – 15.40, Hall 1B

Background
Population estimates of pre-existing mental illness in patients with cancer, their care pathway and outcomes are unknown in the UK. We explore cancer occurrence, stage and survival in psychiatric patients compared to the general cancer population.

Method
Data from the NI Cancer Registry (2009-2011) for patients under 75 were linked to prescribing data and analysed by
drug categories prescribed 3 months before a cancer diagnosis:

1. Anti-psychotic drugs (BNF code 4.2)
2. Hypnotics/anxiolytic or anti-depressant drugs (BNF codes 4.1 & 4.3) but not anti-psychotic drugs.
3. None of the above.

Frequency distributions between different drug categories were compared using z- and Chi-square tests, while survival analysis used the Kaplan-Meier and Cox regression methods.

**Results**

Of 20,426 cancer patients, 7.6% (male: 7.0%, female: 8.1%) received anti-psychotic drugs varying from 3.4% for malignant melanoma to 23% for stomach cancer; 34.9% (male: 29.9%, female: 40.3%) were prescribed hypnotics or anxiolytics and 29.5% (male: 23.3%, female: 36.3%) anti-depressants, while 55.4% (male: 61.1%, female: 49.2%) had no psychiatric drug record. Mental health patients were more likely to be older and economically deprived. Oesophageal, stomach, gallbladder, pancreas, lung, ovary and brain cancers made up higher proportions of cancers diagnosed among mental health patients compared to those on no drugs, whereas non-melanoma skin, melanoma, breast, prostate, testicular and uterine cancer, leukaemia and lymphomas were lower. Patients prescribed anti-psychotic medication were more likely to have stage IV breast and colorectal cancers and lower survival. Breast cancer survival differences were accounted for by age and stage.

**Conclusion**

Cancer patients prescribed anti-psychotic drugs have higher tobacco related and brain cancers, lower skin, breast and prostate cancers, late presentation and lower survival despite frequent service contact. Awareness of cancer in psychiatric patients should be raised among relevant professionals. The poorer survival of this subgroup impacts on overall cancer survival.

**Acknowledgements**

The N. Ireland Cancer Registry is funded by the Public Health Agency, Northern Ireland. Thanks to Business Services Organisation (BSO) for the provision of prescription data for this study.

**Discussion**

15.40 – 16.00

The cancer cell and model systems II

Hosted by Julian Downward, Cancer Research UK London Research Institute, UK

The c-MET-JAK1/2-STAT3 signalling axis is regulated by ADAM17 and is a key mediator of resistance to MEK inhibition in KRAS mutant colorectal cancer

Sandra Van Schaeybroeck, Murugan Kalimutho, Philip Dunne, Wendy Allen, Puthen Jithesh, Cathy Fenning, Robbie Carson, Daniel Longley, Patrick Johnston

Queen’s University Belfast, Belfast, UK

14.30 – 14.40, Room 11

**Background**

Mutations in the KRAS proto-oncogene are found in 40%-45% of colorectal cancer (CRC) patients and confer resistance
to EGFR monoclonal antibody therapies. The identification of druggable targets that uniquely target KRAS mutant (MT) tumours has the potential to fill a gap in the therapeutic armamentarium of advanced CRC.

**Method**

To identify novel targets/pathways which are critical for the survival of KRASMT tumours, both basally and following MEK1/2 treatment, we combined microarray data from isogenic *in vivo* KRAS wild type (WT) and MT CRC models, KRASWT/MT primary tumours, and publicly available datasets.

**Results**

Pathway analysis of the microarray data followed by siRNA screening revealed that JAK1/2-STAT3 signaling is an important pro-survival signal in KRASMT CRC cells. Moreover, suppression of JAK1/2-STAT3 activity using small molecule inhibitors resulted in apoptosis induction in KRASMT CRC cells. In addition, treatment with MEK inhibitors significantly increased JAK2-STAT3 activity in KRASMT but not wild-type models *in vitro* and *in vivo*. c-MET was identified as the upstream receptor that promotes JAK1/2-STAT3-mediated resistance to MEK inhibitors in KRASMT CRC cells. Importantly, ADAM17 was found to mediate this feedback activation of c-MET. Furthermore, combinations of either c-MET or JAK1/2 inhibitors with MEK inhibitors led to marked increases in apoptosis and dramatically attenuated tumor growth *in vivo*. These findings support the clinical assessment of combined JAK1/2-MEK or c-MET-MEK inhibition for the treatment of KRASMT CRC.

**Conclusion**

Using a systems biology approach, we have identified an essential role for c-MET-JAK1/2-STAT3 signaling in KRASMT CRC that support the further clinical development of JAK/STAT3 or c-MET inhibitors in conjunction with MEK inhibition in KRASMT CRC tumours.

**Measurement of the acute response to hypoxia in rat tumours in vivo using magnetic resonance spectroscopy and hyperpolarised pyruvate**

Steven Reynolds, Joanne Bluff, Tooba Alizadeh, Samira Kazan, Stephen Metcalf, Emily Wholey, Leigh Williams, Adriana Bucur, Becky Bibby, Martyn Paley, Gillian M Tozer

University of Sheffield, Sheffield, UK

14.40 – 14.50, Room 11

**Background**

Vascular targeting of tumours represents a proven complementary approach to conventional cancer therapy. Vascular disrupting agents (VDAs) cause extensive oxygen and nutrient deprivation, leading to tumour cell death. Therefore, monitoring oxygenation levels is vital in understanding this process. The influence of tumour oxygenation state on tumour metabolism was determined by administering hyperpolarised $^{13}$C$_1$-pyruvic acid to BDIX rats bearing syngeneic subcutaneous P22 sarcomas and estimating the rate constant for conversion of pyruvate to lactate, $k_{pl}$, using magnetic resonance spectroscopy.

**Method**

Tumor pO$_2$ was manipulated by supplying either normal or hypoxic air (10-15% O$_2$, 4% CO$_2$, balance N$_2$). 5ml/kg of hyperpolarised $^{13}$C$_1$-pyruvate was injected and slice-localised $^{13}$C magnetic resonance (MR) spectra acquired using a $^{13}$C/$^1$H surface coil positioned over the tumour in a 7T MRI system. Pyruvate and lactate integrals versus time were fitted, using Matlab, to a two-way exchange model and $k_{pl}$ values extracted.
Results

$k_{pl}$ significantly increased from 0.031±0.007s$^{-1}$ under normoxia to 0.049±0.019s$^{-1}$ for hypoxic conditions (mean±SD for $n=8$ $p<0.01$). Control experiments of multiple pyruvate injections in air-breathing rats ($n=7$) demonstrated no significant change in the rate constant, $k_{pl}$, between 1st injection (0.046±0.015s$^{-1}$) and 2nd injection (0.051±0.015s$^{-1}$). A significant correlation was also found between $k_{pl}$ versus combined mean arterial blood pressure (MABP) and arterial blood oxygenation, $pO_2$ levels.

Conclusion

MR methods for in vivo monitoring of metabolism of a hyperpolarised substrate (pyruvate to lactate) in tumour tissue were developed. The increase in $k_{pl}$ indicates a shift away from oxidative phosphorylation under hypoxic conditions, suggesting that measurement of this parameter would be useful for monitoring the effects of tumour vascular disrupting agents. The strong correlation between $k_{pl}$ and MABP*pO$_2$ is most likely due to MABP driving tumour blood flow and therefore influencing tumour pO$_2$.

Acknowledgements

Grant funding by Programme Grant C1276/A10345 from Cancer Research UK and EPSRC with additional funding from MRC and Department of Health (England).

References


PTEN phosphatase-independent maintenance of apical membrane integrity during colorectal glandular morphogenesis

Ravi Deevi
Queen’s University of Belfast, Belfast, UK
14.50 – 15.00, Room 11

Background

Disruption of glandular morphogenesis (GM) is a hallmark of high grade, aggressive colorectal cancer (CRC) but causal mechanisms remain unclear. The tumour suppressor PTEN regulates three dimensional (3D) epithelial morphogenesis by coupling the GTPase cdc42 to spatial cues at the apical membrane (AM). PTEN knockdown disrupts AM integrity and induces a glandular phenotype evocative of high grade cancer in a Caco-2 colorectal organotypic model system. While PTEN has phosphatase-dependent and -independent functions, Caco-2 GM is unaffected by oncogenic phosphatidylinositol 3-kinase (PI3K) signalling. The aims of this study were to investigate effects of PTEN functional domains on 3D Caco-2 morphogenesis and to assess model fidelity to human CRC.

Method

GST PAK based cdc42 pull down, transfections, cell culture and three dimensional cultures of cells, confocal microscopy, western blotting and shRNA stable expression.

Results

Here we show that transient expression of either wild type PTEN or PTEN mutants containing an intact C2 domain enhanced cdc42 activity in PTEN-deficient colorectal epithelium cells. Transfection of PTEN-deficient Caco-2 (Caco-2 ShPTEN) cultures with the PTEN C2 domain rescued AM integrity and defective 3D morphogenesis. Conversely, a C2 domain construct mutated at its CBR3 lipid-binding motif was ineffective. Treatment of cells with sodium butyrate
up regulates PTEN expression and also rescued morphogenesis defects in shCaco2 cells. Fundamental attributes of the model system viz associations between AM integrity and gland morphology were conserved and had prognostic significance in CRC. Taken together, these data show that the catalytically inert PTEN C2 domain influences AM dynamics and gland formation in a predictive CRC morphogenesis model system. Insights of PTEN C2-cdc42 pathways of AM integrity may identify molecular therapeutic targets for high grade CRC.

Conclusion
Overall, we conclude that PTEN/Cdc42 pathway regulates apical dynamics thereby epithelial morphogenesis and this pathway may be useful as targets to treat colorectal cancer.

Acknowledgements
We are greatly indebted to Dr T Waldman, Georgetown University for supply of PTEN+/+ and HCT116 cells, Dr A Hall, Sloan-Kettering Cancer Center, NY for PTEN constructs and Dr NR Leslie, University of Dundee for provision of PTEN-C2 constructs.

Parallel functional genetic and compound screens identify WEE1 inhibition as a therapeutic strategy for cancers with defects in Fanconi Anaemia and HR pathways

Marieke Aarts1, Ilirjana Bajrami1, Richard Elliott1, Christopher Lord1, Alan Ashworth1, Nicholas Turner1,2
1Breakthrough Breast Cancer Research Centre, The Institute of Cancer Research, London, UK, 2Breast Unit, Royal Marsden Hospital, London, UK
15.00 – 15.10, Room 11

Background
WEE1 kinase is a critical regulator of mitotic entry through inhibitory phosphorylation of CDK1. We have previously shown that WEE1 inhibitors synergized with DNA damaging agents that arrested cells in S-phase, triggering direct mitotic entry without completing DNA synthesis, resulting in catastrophic chromosome fragmentation and apoptosis.

The aim of this study was to understand how forced mitotic entry could be best exploited for cancer therapy, and to identify novel determinants of sensitivity to WEE1 inhibition.

Method
We performed a functional genetic screen with an siRNA library targeting the kinome, phosphatome, DNA repair and tumour suppressor genes to identify genes and pathways whose inhibition synergized with WEE1 inhibitor MK-1775. In parallel, a library of drugs and kinase inhibitors was screened. The underlying mechanism of sensitivity or resistance was studied for selected hits.

Results
Drug and siRNA screening identified synergy between WEE1 and CHK1 inhibition, and WEE1 inhibition and MYT1 depletion, with the combinations forcing S-phase cells directly into mitosis. Silencing of multiple DNA helicases and components of the Fanconi anaemia (FA) and homologous recombination (HR) pathways sensitised to MK-1775, which was accompanied by increased gamma H2AX induction in S-phase and premature mitotic entry.

Conclusion
Through parallel compound and functional genetic screens we have identified novel combinations that induce mitotic entry of S-phase cells in the absence of chemotherapy. Our results suggest that cancers with defects in FA and HR pathways may be targeted by WEE1 inhibition, providing a basis for a novel synthetic lethal strategy for cancers harbouring FA/HR defects.
The role of JAK1/2-STAT3 as acute resistance mechanism to MEK inhibition in BRAF mutant colorectal cancer cell lines

Basak Celtikci, Robert Carson, Sandra Van Schaeybroeck, Patrick Johnston

Queen’s University Belfast, UK
15.10 – 15.20, Room 11

Background
Oncogenic mutations in BRAF occur in 8% of patients with advanced colorectal cancer (CRC) and have been shown to correlate with poor prognosis. In contrast to BRAF mutant (MT) melanoma, where the BRAF inhibitor Vemurafenib (PLX4032) has shown significant increases in response rates and overall survival, only minor responses to Vemurafenib treatment have been reported in BRAFMT CRC. Clear understanding of the vulnerabilities of BRAFMT CRC is important, and identification of druggable targets uniquely required by BRAFMT CRC tumours has the potential to fill a gap in the therapeutic armamentarium of advanced CRC. The aim of this study was to identify novel resistance mechanisms to Vemurafenib treatment in BRAFMT CRC.

Method
Paired BRAFMT/WT RKO and VACO432 CRC cell line models and non-isogenic BRAFMT LIM2405, WiDR, HT-29 and COLO205 CRC cells were used. Changes in protein expression/activity were assessed by Western Blotting. Interaction between MEK1/2 and JAK1/2 inhibition was assessed using the MTT cell viability assays and Flow Cytometry. Apoptosis was measured using Western Blotting for PARP, cleaved caspase 3/8, caspase 8 and 3/7 activity assays.

Results
Treatment with MEK1/2 inhibitors AZD6244, trametinib, UO126 and PD98059 resulted in acute increases in STAT3 activity in the BRAFMT RKO and VACO432 cells but not in their BRAFWT clones and this was associated with increases in JAK2 activity. Inhibition of JAK/STAT3 activation using gene specific siRNA or small molecule inhibitors TG101348 or AZD1480, abrogated this survival response and resulted in significant increases in cell death when combined with MEK1/2 inhibitors AZD6244 or trametinib in BRAFMT CRC cells. In addition, combination of MEK1/2 and JAK/STAT3 inhibition resulted in strong synergy with CI values between 0.3 and 0.7 in BRAFMT CRC cells.

Conclusion
We have identified JAK/STAT3 activation as an important escape mechanism for BRAFMT CRC following MEK1/2 inhibition in vitro. These data provide a strong rationale for further investigation of combination of MEK1/2 and JAK/STAT3 inhibition in BRAFMT in vivo models.

Replication stress links structural and numerical cancer chromosomal instability

Rebecca Burrell¹, Sarah McClelland¹,², David Endesfelder¹,², Petra Groth³, Marie-Christine Weller³, Nadeem Shaikh¹, Enric Domingo⁴, Nnennaya Kanu¹,⁵, Sally Dewhurst¹, Eva Gurooos³, Su Kit Chew¹,⁵, Andrew Rowan¹, Arne Schenk², Michal Scheffer⁶, Michael Howell¹, Maik Kschischo⁷, Axel Behrens¹, Thomas Helleday¹, Jiri Bartek⁷,⁸, Ian Tomlinson⁴

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15.20 – 15.30, Room 11

Background
Cancer chromosomal instability (CIN) results in an increased rate of change of chromosome number and structure and
generates intratumour heterogeneity. CIN is observed in most solid tumours and is associated with both poor prognosis and drug resistance. Understanding a mechanistic basis for CIN is therefore paramount.

**Method**

We combined genomics approaches with classical cell biology and high-resolution microscopy, in addition to DNA fibre assays in tissue culture cells.

**Results**

We find evidence for impaired replication fork progression and increased DNA replication stress in CIN+ colorectal cancer (CRC) cells relative to CIN- CRC cells, with structural chromosome abnormalities precipitating chromosome missegregation in mitosis. We identify three new CIN-suppressor genes (PIGN (also known as MCD4), MEX3C (RKHD2) and ZNF516 (KIAA0222)) encoded on chromosome 18q that are subject to frequent copy number loss in CIN+ CRC. Chromosome 18q loss was temporally associated with aneuploidy onset at the adenoma–carcinoma transition. CIN-suppressor gene silencing leads to DNA replication stress, structural chromosome abnormalities and chromosome missegregation. Supplementing cells with nucleosides, to alleviate replication-associated damage, reduces the frequency of chromosome segregation errors after CIN-suppressor gene silencing, and attenuates segregation errors and DNA damage in CIN+ cells.

**Conclusion**

These data implicate a central role for replication stress in the generation of structural and numerical CIN, which may inform new therapeutic approaches to limit intratumour heterogeneity.

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**Signalling pathways required for Normal Fibroblast (NF) to Cancer-Associated Fibroblast (CAF) conversion**

**Nil Ege, Fernando Calvo, Erik Sahai**

Cancer Research UK London Research Institute, London, UK

15.30 – 15.40, Room 11

**Background**

The microenvironment of the tumour or stroma is a complex network of different cell types. Cancer-associated fibroblasts (CAF) are one important population present in the stroma. As well as producing the extracellular matrix, they are key regulators of paracrine signalling between stromal and cancer cells. Several studies have investigated their origin, one hypothesis being that they arise from the conversion of resident normal fibroblasts (NF). However the molecular and functional differences between normal and cancer-associated fibroblasts have yet to be fully determined.

**Method**

Gene set enrichment analysis was completed to identify signaling pathways up-regulated in CAF compared to NF. Reporters to track transcriptional activities and protein localisations of these pathways are used for live cell imaging both in vitro and in vivo.

**Results**

Genomic analyses suggested that YAP, SRF and TGFbeta pathways are up regulated in CAF compared to NF. This was then confirmed by QPCR analysis studying the expression levels of target genes.

We have further identified several cytoskeletal regulators (such as ANLN, DIAPH3 or MYL9) specifically regulated by YAP and required for CAF functionality in organotypic cultures (Calvo et al.).

We are now testing the dynamic and specificity of our constructs to report transcriptional activities and protein
localisation of YAP, SRF and TGFbeta pathways. We aim to use those reporters to visualise pathways activities in vitro and in vivo and to understand their chronology and their possible interdependence during fibroblast conversion.

**Conclusion**

In this project we have documented the role of YAP signaling pathway in CAF function. In parallel we set up several tools to further image in vitro and in vivo these three pathways activity during the activation and maintenance of CAF.

**References**


**Discussion**

15.40 – 16.00

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**Diagnosis and therapy**

**Hosted by Patrick Johnston, Queen’s University Belfast, UK**

**ACP McElwain Award winner: Antibodies of the IgE class: Preclinical evaluations for therapeutic use in the treatment of solid tumours**

**Debra Josephs**

King’s College London and Guy’s and St Thomas’ Hospitals, London, UK

14.30 – 14.45, Room 3A

All antibody cancer therapeutics rely on only one class, namely IgG. Although efficacious, IgG binds with low affinity to immune cell receptors and is subject to inhibitory mechanisms. Other antibody classes, namely IgE, may demonstrate superior tissue bioavailability and higher receptor affinity, which may in turn result in improved efficacy. MOv18 IgE against the ovarian carcinoma antigen, folate receptor alpha (FRα) is a novel system to model this hypothesis.

A safety concern for IgE immunotherapy is induction of effector cell activation (anaphylaxis) in the circulation. To assess this, two model systems were adopted. One measured release of a granule-stored mediator from a basophilic cell line (RBLSX-38); the other measured CD63 expression, a marker of activation on blood basophils. MOv18 IgE alone, or with recombinant FRα, healthy volunteer or ovarian carcinoma patient sera, did not induce RBLSX-38 degranulation. In addition, MOv18 IgE did not induce CD63 expression on basophils from healthy volunteers or cancer patients, despite detectable circulating FRα. Exposure to FRα-expressing tumour cells, however, at target-to-effector ratios expected within tumours, induced degranulation.

To examine the efficacy and safety of MOv18 IgE, an immunocompetent surrogate rat model of FRα-expressing carcinoma was developed. Surrogate rat-MOv18 IgE and IgG2b antibodies were cloned, expressed and purified, and both demonstrated functionality. Systemic administration of MOv18 IgE and IgG2b at doses of 1-50mg/kg demonstrated significantly superior efficacy of MOv18 IgE compared to IgG2b. Furthermore, administration of MOv18 IgE for the first time in an animal expressing the full complement of IgE-receptor-expressing immune cells revealed no additional clinical nor histopathological toxicities compared to IgG2b. Finally, in vivo, ex vivo and in vitro assays revealed important roles for tumour-associated-macrophage activatory and migratory pathways, including upregulation of a unique cytokine signature. These findings are of pivotal significance to the translation of the first IgE class antibody towards first-in-human clinical trials.
The development of cutaneous squamous lesions in patients treated with vemurafenib: A possible role for human papillomavirus in addition to activated RAS

Karin Purdie1, Andrew South2, Mary Sommerlad3, Hasan Rizvi3, Irene Leigh2, Charlotte Proby2, Catherine Harwood1,3

1Centre for Cutaneous Research, Blizard Institute, Queen Mary University of London, London, UK, 2Division of Cancer Research Jacqui Wood Cancer Centre, Ninewells Hospital and Medical School, Dundee, UK, 3Department of Dermatology, Barts Health NHS Trust, London, UK

14.45 – 14.55, Room 3A

Background
Approximately half of metastatic melanomas have an activating mutation in the BRAF oncogene. The BRAF inhibitor vemurafenib is associated with the de novo development of benign and malignant squamoproliferative lesions in up to 25% of patients. The putative mechanism involves paradoxical increased MAPK signalling by BRAF inhibitors in the context of mutated or activated RAS. However, cutaneous SCC (cSCC) have been reported to develop in association with wart-like lesions and upregulation of the MAPK pathway is known to facilitate human papillomavirus (HPV) replication, suggesting a possible role for HPV in the pathogenesis of these lesions.

Method
We have examined RAS mutational status and presence of HPV DNA in 30 skin biopsies from 4 patients receiving vemurafenib (20 benign squamoproliferative lesions; 7 SCC; 3 normal skin samples).

Results
A high proportion (90%; 27/30) were positive for beta (EV-associated) HPV; a subset (15%; 4/27) were also positive for cutaneous alpha HPV. HPV DNA was detected at high levels in only a minority (19%; 5/27) of positive lesions, all of which were identified clinicopathologically as viral warts. HRAS mutations were detected in 8/20 (40%) samples (6/16 benign squamoproliferative lesions and 2/3 cSCC). No mutations were identified in the NRAS or KRAS genes. Five of 8 (63%) HRAS mutations were in codon 61, a mutational hotspot previously reported as characteristic of vemurafenib-associated cSCC.

Conclusion
The high frequency of HRAS mutations in our sample series together with the rapid timeframe of their development support the hypothesis that these mutations are pre-existing and confer a selective advantage in the context of vemurafenib therapy. The role of HPV in these lesions merits further investigation.

How does RAS contribute to cutaneous squamous cell carcinoma?

Angela McHugh1, Mark Saville1, Catherine Harwood2, Karin Purdie2, Alan Evans3, Aidan Rose1, Colin Fleming4, Irene Leigh1, Andrew South1, Charlotte Proby1

1Division of Cancer Research, Ninewells Hospital & Medical School, University of Dundee, Dundee, UK, 2Centre for Cutaneous Research, Barts and the London Queen Mary University of London, London, UK, 3Department of Pathology, Ninewells Hospital & Medical School, Dundee, UK, 4Department of Dermatology, Ninewells Hospital, Dundee, UK

14.55 – 15.05, Room 3A

Background
Cutaneous squamous cell carcinoma (cSCC), the second most common skin cancer, is a major problem in our ageing population. In Scotland, there has been a 55% increase in cSCC incidence in the decade 2000-2010, with a 50% increase in workload for UK dermatologists predicted by 2030. TP53 and NOTCH genes are identified as important tumour suppressors, but critical oncogenes for cSCC are yet to be defined. Activating mutation in HRAS is the initiating
event in the mouse chemical carcinogenesis model but, in mouse and human xenograft models of cSCC, oncogenic ras alone is insufficient for invasive malignancy and additional genetic manipulation is necessary. The role of oncogenic ras in human cSCC is even less clear, but has clinical relevance given the therapeutic potential for targeting MAPK and PI3K signaling with inhibitors.

Method
Whole exome sequencing of 20 cSCC was undertaken using Agilent exome capture arrays sequenced on the Illumina Hi-Seq platform, with validation in 82 cSCC (DNA amplified on the Fluidigm Access Array and sequenced using the Roche 454 Junior System).

Results
Activating mutations of RAS were present in 11% of 102 cSCC. The frequency was 3-fold higher (35%) in an additional 20 squamous neoplasms arising in the context of vemurafenib treatment for BRAF-mutant melanoma, suggesting RAS mutation may be a frequent event in human keratinocytes, but often will not progress to invasive SCC due to oncogene-induced senescence. NOTCH1 was the only known cancer driver, other than RAS, significantly mutated in vemurafenib-tumours (60%) and activating RAS mutation co-segregated with NOTCH1 mutation in the validation cohort of 82 cSCC.

Conclusion
These data suggest that suppression of NOTCH1 is important for ras-driven clonal proliferation. Kinase inhibitors alone and in combination are being used to dissect the ras pathway-dependency of a panel of cSCC cell lines.

Acknowledgements
This work was funded by Cancer Research UK and the British Skin Foundation.

Changes in glutathione metabolism mediate the resistance of EGFR-T790M mutant lung cancer cells to erlotinib
William B Stokes1, Hongde Li2, Rajat Roy1, Emily Chater1, Michael Seckl1, Yulan Wang2, Huiru Tang2, Olivier E Pardo1
1Imperial College London, London, UK, 2Chinese Academy of Sciences, Wuhan, China
15.05 – 15.15, Room 3A

Background
EGFR tyrosine-kinase inhibitors (eg. erlotinib) are novel agents in the treatment of EGFR-dependent lung cancer. However, their long-term efficiency is impaired by the development of drug-resistance through secondary receptor mutations (eg T790M). Although decreased affinity of the mutants for the inhibitors was suggested to be responsible for this, we show that additional factors are at play.

Method
We used 1H-NMR metabonomics profiling of erlotinib-sensitive/resistant cell pairs to identify metabolic pathways modulated during acquisition of resistance to EGFR TKIs. We then validated one of the pathways identified, using biochemical and molecular biology methods to highlight how these metabolic changes were acquired by T790M erlotinib-resistant cells.

Results
We found that the levels of 13 metabolites were significantly altered in association with TKIs sensitivity, with GSH being considerably reduced in erlotinib-resistant (ER) cells. Using RNA interference, as well as pharmacological inhibitors of GSH pathway enzymes, we demonstrate that increasing GSH levels in ER cells sensitises these to erlotinib. Conversely, reducing the intracellular concentration of GSH renders sensitive cells resistant to the drug. Using qPCR, we show that
the reduction in GSH levels in ER cells is associated with the decreased expression of the GSH synthesis enzymes, GCLC and GSS. This correlates with inhibition of NRF2, through increased KEAP1 levels and/or decreased expression of SQSTM1 and PALB2. We demonstrate these changes to be directly linked to acquisition of the T790M mutation, as transfection of this mutant EGFR in HEK293 cells causes a drop in GSH levels and decreased expression of both SQSTM1 and PALB2. Finally, administration of ethacrynic acid, a GST inhibitor that increases intracellular GSH levels, re-sensitises resistant tumours to erlotinib in a xenograft mouse model.

Conclusion
Taken together, our data identify a new resistance mechanism to EGFR TKIs and propose a novel therapeutic strategy to tackle this problem in the clinic.

Clinical outcome following video-assisted thoracoscopic surgery (VATS) or thoracotomy in the surgical management of lung cancer: A multicentre UK analysis from 2001-2013

Jason Sangha¹, Felicity Evison², Daniel Ray², Paul Moss²
¹University of Birmingham, Birmingham, UK, ²University of Birmingham, University Hospitals Birmingham NHS Foundation Trust and Birmingham CRUK Centre, Birmingham, UK
15.15 – 15.25, Room 3A

Background
The role of video-assisted thoracoscopic surgery (VATS) in the routine management of early stage non-small cell lung cancer (NSCLC) remains controversial. Concerns about operative safety and the oncological adequacy of VATS compared to thoracotomy have limited the uptake of VATS as a surgical approach towards NSCLC. We have compared the demographic profiles and clinical outcome of patients with lung cancer treated with VATS or thoracotomy.

Method
We utilised data from the Hospital Episode Statistics (HES) database of inpatients in England. The ICD-10 classification was used to identify patients with a diagnosis of lung cancer and OPCS codes identified the surgical procedure used to treat the malignancy. Data were then extracted into SPSS for statistical analysis. For all reported analyses, $p \leq 0.001$.

Results
During 2001-2013 we identified 36,400 patients having undergone surgery for lung cancer. Of these, 32,470 (90%) underwent thoracotomy whereas 3617 (10%) were treated with VATS. Patients undergoing VATS were significantly older (68.6 vs. 66.6yrs), from a less deprived area, had a higher Charlson comorbidity index (4.94 vs. 4.56), shorter duration of hospital stay (7.94 vs. 10.9 days), and were less likely to be readmitted within 28 days (0.4% vs. 5.6%). Post-operative mortality at 30 days was lower with VATS (1.6% vs. 3.1%) and Kaplan-Meier survival analysis demonstrated improved survival with VATS, with a median survival of 6.12yrs compared to 4.80yrs with thoracotomy. Cox regression incorporating age and Charlson comorbidity index found VATS was associated with improved survival, with a hazard ratio of 0.726 (95% CI: 0.677-0.778).

Conclusion
To our knowledge, this is the largest study to have compared outcomes between VATS and thoracotomy. We conclude that VATS is a safe and effective procedure for the treatment of NSCLC. Comparative multicentre studies incorporating staging information are urgently required to further evaluate VATS.
The glycoprotein, Decorin is a novel anti-proliferative and anti-angiogenic treatment for glioblastoma multiforme

Hannah Shereef¹, Lisa Hill¹, Kismet Hossain-Ibrahim², Roy Bicknell², Ann Logan¹, Garth Cruickshank²

¹School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK, ²Department of Neurosurgery, University Hospitals Birmingham, Birmingham, UK

TUESDAY 4

Background

Glioblastoma multiforme (GBM) is the commonest and most malignant primary brain tumour in adults. Its prognosis remains poor with current treatment options. Existing targeted agents such as bevacizumab, a monoclonal antibody to VEGF-A, have had limited efficacy due to inherent and acquired resistance - probably as a result of redundancy in biological systems promoting GBM growth and angiogenesis. Decorin, a naturally occurring proteoglycan, antagonises several growth factors such as VEGF(1) and TGF-β(2) and receptor tyrosine kinases such as EGFR(3) and c-Met(4), which positively regulate GBM growth and angiogenesis. We hypothesised that Decorin inhibits growth and angiogenesis in GBM by blocking multiple signalling pathways. We have available to us GCP-grade human recombinant Decorin; we aimed to test our hypothesis by administering this in a pre-clinical model of GBM.

Method

An in vivo tumour xenograft model of U-87 MG (human glioma) cells was developed in immunocompromised mice. Tumours identical in size were administered Decorin or PBS (control) locally to the tumour site every 24 hours for 8 days. Tumour sizes were measured prior to each treatment dose. Immunohistochemistry was done on excised tumour tissue to quantify proliferating cells and blood vessel density.

Results

Decorin-treated GBM tumour xenografts had a substantially slower growth rate compared to PBS-treated tumours (mean tumour volume 389mm³ vs 816mm³ at end of treatment period) (p<0.001, n=5 per treatment group). Immunohistochemistry revealed a 2.8-fold reduction in proliferating cell density and 2-fold reduction in vascular density in Decorin-treated tumour sections compared to PBS-treated tumour sections.

Conclusion

Decorin inhibits GBM growth and angiogenesis. Decorin’s combinatorial mode of action, by inhibiting several signalling pathways involved in both processes, make it an exciting and novel candidate for targeted therapy in GBM, and one that is less susceptible to resistance. Further work will confirm its mechanism of action in GBM and take the drug into clinical trials.

References


**Preliminary results of the GALA-5 study: an evaluation of the tolerability and feasibility of combining 5-Amino-Levulinic Acid (5-ALA) with carmustine wafers (Gliadel) in the surgical management of primary glioblastoma**

**Colin Watts¹**, **Katharina Wanek²**, **Nicolas Counsell²**, **Paul Smith²**

¹University of Cambridge, Cambridge, UK, ²UCL Clinical Trials Unit, London, UK

15.35 – 15.45, Room 3A

**Background**

Objective: to establish the safety and tolerability of combining fluorescence-guided surgical resection (5-ALA) with intra-operative chemotherapy (carmustine wafers) in patients with primary glioblastoma prior to standard treatment with radiotherapy and temozolomide

**Method**

A single arm design with the following inclusion criteria:

- Age 18+ years
- Patient reviewed at a specialist neuro-oncology MDT
- Imaging evaluated by a neuro-radiologist and judged to be a GBM
- Radical resection judged to be realistic by the neurosurgeons (i.e. NICE criteria for the use of Carmustine wafers can be met)
- WHO performance status 0 or 1 on clinical review

**Results**

Seventy-two patients were recruited from 8 sites between August 2011 and May 2013; 64 patients received carmustine wafer implants and 59 patients were found to be eligible after surgery. Thirteen patients were found to be ineligible due to: wafers not inserted (n=8); GBM not diagnosed post-operatively (n=4); simultaneous diagnosis of unrelated cutaneous sebaceous carcinoma (n=1).

There were 8 surgical complications in 6 eligible patients (10%): wound infections were reported in 5 patients (8%) and cerebrospinal fluid leakage in 3 patients (5%). One patient was not able to begin chemoRT (1/31, 3%), and 3 patients (3/31, 10%) were not able to begin chemoRT within 6 weeks of surgery, due to surgical complications.

After a median follow-up of 6.6 months, 36 patients (61%) are alive without progression, 8 patients (14%) are alive having progressed and 15 patients (25%) have died. Thirty patients (51%) have reported 61 adverse events of grade 3 or higher, the most common of which was muscle weakness reported in 5 patients (8%).

**Conclusion**

The combination of 5-ALA and carmustine wafers is safe and tolerable in the surgical management of primary glioblastoma. A phase III randomised controlled trial is being designed to test efficacy of the combination.
Proffered paper session abstracts

Discussion
15.45 – 16.00

Radiotherapy and radiobiology

Hosted by Diana Tait, The Royal Marsden NHS Foundation Trust and Dean, The Royal College of Radiologists, London, UK

Simultaneous cone beam CT scanning during prostate radiotherapy produces clinically useful images
Peter Dickinson, Julie Stratford, Chris Boylan, Carl Rowbottom, Ananya Choudhury
The Christie NHS Foundation Trust, Manchester, UK
14.30 – 14.40, Hall 1A

Background
Calculations performed on a single radiotherapy planning CT scan do not accurately represent dose delivery during prostate radiotherapy because of inter- and intra-fraction organ motion. Cone beam CT (CBCT) scanning during the delivery of arc radiotherapy allows organ motion to be monitored. We studied the quality of simultaneous CBCTs.

Method
Forty-nine patients with localised prostate cancer were treated with radical VMAT radiotherapy. Treatment was delivered using a single 8 or 10 MV arc. Standard and simultaneous CBCT’s were captured on fractions 1, 6, 11 and 16. The quality of each CBCT image was assessed independently by a clinician and a radiographer using a validated scoring tool. The observers were blinded to whether the scan was a standard or simultaneous CBCT.

Results
392 CBCT scans were performed on 49 patients. 74 simultaneous CBCT scans were performed with a mean arc delivery time of 120 seconds during which 688 CBCT frames were acquired. Following a software upgrade the subsequent 122 simultaneous CBCTs were obtained with a mean arc delivery time of 83 seconds during which 502 CBCT frames were acquired.

There was moderate agreement in image quality scores between the two observers (kappa statistic 0.44). The independent observers agreed that 193 (98%) standard CBCT images and 99 (51%) simultaneous CBCTs were clinically useful. Following the software upgrade the proportion of simultaneous CBCTs which were deemed clinically useful fell from 93% to 67% and from 95% to 85% for observers 1 and 2 respectively.

Conclusion
Simultaneous CBCT scanning can produce clinically useful images. These images could be used to more accurately model the actual dose received by the prostate, rectum and bladder during prostate radiotherapy. Factors which potentially affect simultaneous CBCT image quality include gantry speed, treatment beam energy, CBCT imaging dose and number of CBCT frames acquired. The simultaneous CBCT technique warrants further development.
FDG-PET parameters as predictors for outcome in non small cell lung cancer (NSCLC) treated with stereotactic body radiotherapy (SBRT)

Mymoona Alzouebi1, Manil Subesinghe2, S Ramasamy1, Michael Snee1, Robert Turner1, Robert Stuart1, Kevin Franks1, Helene Thygesen3, Katy Clarke1

1St James’s University Hospital, Leeds, UK, 2Leeds Teaching Hospital, Leeds, UK, 3University of Leeds, Leeds, UK

14.40 – 14.50, Hall 1A

**Background**

To identify predictive FDG-PET imaging factors for outcomes following SBRT in early stage NSCLC

**Method**

Patients with inoperable T1 and T2 NSCLC and a baseline FDG PET-CT at a single centre (St James’s University Hospital, Leeds, UK) treated with SBRT for a single tumour between 2009 and 2012 were included. Scans were reported by a single radiologist. Prospective data was collected on a range of FDG-PET parameters (including SUVmax and TLG — Total lesion glycolysis). Patient characteristics and outcome variables including stage, histology, PTV volume, performance status, dose, time interval between PET and SBRT, maximum response to treatment and patterns of failure collected and analysed. The PET parameters were analysed as a continuous variable.

**Results**

125 patients (72 female, 53 male), median age 75.2. 94 were T1 and 31 T2. Median follow up 1.19 yrs (range 0.28-3.3). Histology was available in 40 patients.

In assessable patients maximal response to treatment was CR in 19%, PR in 50%, SD in 14% and PD in 11%.

Relapse free survival at 2 years was 55%. Local, regional and distant relapse-free rates were 94%, 89% and 83% respectively. Overall and cause-specific survival at 2 years was 57% and 81% respectively.

Median SUVmax was 9.2 in patients who had a relapse and 7.35 in those without. On multivariate analysis, pre-treatment SUVmax predicted for recurrence (p=0.005528), distant metastases (p=0.024081) and overall survival (p=0.000253). This was consistent amongst patients with and without diagnostic pathology. Median SUVmax for patients with and without histology was 5.85 and 7.65 respectively. SUVmax however did not correlate with local or regional relapse.

Stage was a significant predictor for OS and RFS, consistent with previous data. Dose of radiation and time interval from PET to SBRT showed no significant correlation with outcome.

Other PET parameters assessed include TLG 20 which correlates with regional relapse, the significance of this is not clear.

**Conclusion**

This study identifies that SUVmax is the strongest FDG-PET parameter to correlate with outcome following SBRT for NSCLC. This is consistent with previously published data. With SBRT an emerging treatment modality for early stage disease, this may have future implications on the use of adjuvant chemotherapy.
Does the incidental coverage of axillary nodes by either standard breast or high tangential radiotherapy fields explain Z0011 trial results?

Marjory Maclennan, Sanjana Masinghe, Barbara Cadwallader, Josie Cameron, Avril Middleton, Carolyn Bedi, Tamasin Evans
Edinburgh Cancer Centre, Edinburgh, UK
14.50 – 15.00, Hall 1A

Background
In early breast cancer, axillary node clearance (ANC) or nodal irradiation following positive sentinel lymph node (SLN) biopsy provide equivalent local control. The ACOSOG Z0011 trial demonstrated equivalent survival and locoregional recurrence in patients with positive SLNs offered either ANC or no further axillary treatment. Incidental irradiation of axillary nodal levels by breast tangential fields (TF) may explain these results. Oncologists in Z0011 may have used ‘high tangents (HTs)’, planned by altering the superior field border, with the intention of including the lower nodal levels. These details are unpublished.

Our purpose was to evaluate the volume of axillary nodes encompassed and the dose delivered to each level using both our standard and a high tangential field set up.

Method
Levels 1, 2 and 3 axillary nodes were retrospectively outlined on axial CT simulation images of 50 pts who received standard whole breast irradiation alone following breast conserving surgery. Each patient was planned using both standard TFs and HTs. Dose-volume histograms were used to calculate the percentage volume receiving 95% of the dose (V95%) and the mean dose [D mean (Gy)] of each nodal level.

Results
• Mean dose to each axillary node level was substantially lower than that considered therapeutic even using a modified high tangential field set up (Dmean level 1 = 27.6Gy using standard fields, 35.5Gy with HTs).

• Levels 1 and 2 were only partially included in standard and high tangential field set up. Level 1 V95% = 16% using standard fields and 29% with HTs. Level 2 V95% = 2.91% with standard fields and 8.38% using HTs.

• Large interpatient variation in V95%.

• Level 3 V95% was 0% for all patients.

Conclusion
We suggest the use of ‘HTs’ cannot adequately explain the results of Z0011. Until more information is available on the radiotherapy delivered we cannot assume its impact upon the results.

References
A significant reduction in positive circumferential margin involvement is achieved by combining a low rectal cancer MRI staging system with clinical assessment and sound patient management: experience from the MERCURY II Low Rectal Cancer Study

Nick Battersby¹, Peter How¹, Phil Quirke¹, Brendan Moran¹, Gina Brown², The Mercury II study group¹

¹Pelican Cancer Foundation, Basingstoke, UK, ²The Royal Marsden Hospital, London, UK, ³St James’ Hospital, Leeds, UK

15.00 – 15.10, Hall 1A

Background
A low rectal cancer MRI staging system was retrospectively shown to identify tumours with a threatened circumferential resection margin (CRM). This staging system was used along side clinical assessment in a prospective study in order to selectively use neoadjuvant treatment and to guide the surgical plane. The primary aim of MERCURY II was to reduce the rate of positive circumferential resection margins.

Method
The positive CRM rate was compared between 101 patients from MERCURY I low rectal cancer subgroup and 203 patients from MERCURY II study: combined median age 68, female 112/304 (36.8%). Patient demographics, tumour stage and site, neoadjuvant treatment, operative approach, MRI and pathological findings were recorded.

Results
Median tumour height for MERCURY I subgroup 3.8cm versus MERCURYII 4cm, (p=0.18). The circumferential resection margin was positive in 27/101 (26.8%) MERCURYI subgroup compared with 19/203 (9.4%) MERCURY II (p<0.001). Sphincter sparing surgery was performed in 31/101 (30.7%) compared with 84/203 (41.4%), for MERCURY I subgroup and MERCURY II group respectively (p=0.79).

Conclusion
Combined clinical assessment with the low rectal cancer MRI staging system enabled selective treatment, with a significant overall reduction in circumferential resection margin involvement.

Increased blood flow to human rectal cancer induced by nelfinavir and radiotherapy

Esme Hill¹,², Jamie Franklin², Mike Partridge¹, Somnath Mukherjee¹,², Jun Li¹, Kwun-Ye Chu², Mark Anderson¹,², Ricky Sharma¹,²

¹University of Oxford, Oxford, UK, ²Churchill Hospital, Oxford, UK

15.10 – 15.20, Hall 1A

Background
In preclinical models, nelfinavir, an inhibitor of Akt in the PI3-kinase signalling pathway, is an intrinsic radiosensitiser which increases tumour blood flow and reduces hypoxia. We conducted a pilot study of nelfinavir and short-course pelvic radiotherapy (SCRT) in patients with metastatic rectal cancer to explore changes in tumour perfusion during therapy using perfusion Computed Tomography (pCT).

Method
Eight patients with T3-4 N1-2 M1 rectal cancer received 25 Gy in 5 fractions in 7 days to the pelvis; nelfinavir 1250 mg bd PO was given for 7 days before and 7 days concomitant with RT. pCT scans of the pelvis were performed pre-treatment, on the seventh day of nelfinavir and on the last day of radiotherapy and nelfinavir. Blood Volume (BV), Blood Flow (BF) and Mean Transit Time (MTT) were derived within the tumour region of interest (ROI) on 8 pCT slices using proprietary software (CT Perfusion 3, GE). CT images were used to identify slices from comparable anatomical levels in the pelvis on sequential scans and the mean of the parameter values from those slices was calculated.
Results
All patients completed 3 pCT scans. One patient was excluded from analysis due to technically inadequate scans. On analysis of evaluable scans at baseline and after 7 days of nelfinavir, no statistically significant change was demonstrated. Between the second and third scans there was a median 30% increase in BF (P=0.028) and 24.0% decrease in MTT (P=0.018) [Wilcoxon Signed Ranks Test]. Of note, BF increased in all patients except one, who had progressive disease on pelvic MRI 8 weeks post-SCRT.

Conclusion
SCRT with concurrent nelfinavir results in increased BF and reduced MTT in rectal cancer, indicating improved tumour perfusion. This study is the first to demonstrate an increase in rectal tumour BF on pCT during radiotherapy.

Acknowledgements
NIHR BRC Oxford, ECMC, OCIC, OHSRC.

An evidence-based UK IMRT solution for anal cancer: the development of the control arm for future UK led clinical trials
Rebecca Muirhead1, Richard A Adams2, Duncan C Gilbert3, Mark Harrison4, Robert Glynne-Jones4, David Sebag-Montefiore5, Maria A Hawkins1
1Gray Institute for Radiation Oncology & Biology, Oxford, UK, 2School of Medicine, Cardiff University, Cardiff, UK, 3Sussex Cancer Centre, Royal Sussex County Hospital, Brighton, UK, 4Mount Vernon Hospital, Northwood, UK, 5University of Leeds, St James Institute of Oncology, Leeds, UK
15.20 – 15.30, Hall 1A

Background
Chemoradiation (CRT) is standard treatment for anal cancer achieving loco-regional control and preservation of anal function without a colostomy. Previous phase III trials including ACT2 used relatively crude radiotherapy techniques that cause acute and late radiation morbidity and may contribute to treatment failure due to treatment breaks [1]. An evidence-based IMRT solution is required to form the control arm for future UK anal cancer trials that can test the benefit from dose-escalation to the gross tumour and areas of nodal spread.

Method
We conducted a systematic PubMed/MEDLINE and Embase database search of Anal Cancer IMRT full articles and abstracts published since 2005. Dose fractionation to the gross tumour volume and nodes and elective nodal irradiation were reviewed and compared with the previous ACT2 technique.

Results
Representatives from six centres reviewed the results and held three face to face meetings. A single phase IMRT approach is recommended performed in the supine position with I.V. contrast. Radiobiological modelling was used to derive a continuous single phase solution similar to the approach used in ACT 2. Recommended gross tumour volumes doses to the primary are 50.4Gy in 28 fractions (F) for T1/2 and 53.2Gy in 28GF to T3/4N+ disease. The elective nodal irradiation dose is 40Gy in 28 fractions. Planning objectives and constraints are similar to those used by the RTOG 0529 phase II study [2]. A further five centres reviewed the draft protocol leading to minor modifications.

Conclusion
We present an evidence-based UK Anal IMRT consensus protocol that is suitable for use as the control arm of future UK - led anal cancer trials and routine clinical practice.
References


Preoperative chemoradiation (CRT) with concurrent cetuximab, irinotecan and capecitabine in MRI-defined locally advanced rectal cancer (LARC) within the phase II EXCITE trial: Relationship of epidermal growth factor receptor (EGFR) pathway mutations to histological response and survival

Simon Gollins¹, Nick West¹, Phil Quirke³, Arthur Sun Myint³, Mark Saunders², Shabbir Susnerwala³, David Sebag-Montefiore², Sharadah Essapen⁶, Les Samuel⁷, Bruce Sizer⁷, Sandy Beare⁹, Emma Lawrie⁹, Mark Jitlal⁹

¹North Wales Cancer Treatment Centre, Denbighshire, UK, ²Leeds Teaching Hospitals NHS Trust, Leeds, UK, ³Clatterbridge Cancer Centre, Bebington, UK, ⁴Christie NHS Foundation Trust, Manchester, UK, ⁵Rosemere Cancer Centre, Preston, UK, ⁶St Lukes Cancer Centre, Guildford, UK, ⁷Aberdeen Royal Infirmary, Aberdeen, UK, ⁸Essex County Hospital, Colchester, UK, ⁹Cancer Research UK & UCL Cancer Trials Centre, London, UK

15.30 – 15.40, Hall 1A

Background

A preoperative cetuximab-containing CRT regimen in LARC was examined, including the influence of EGFR pathway mutations.

Method

Patients with MRI-defined LARC threatening/involving potential circumferential resection margin received pelvic radiotherapy (RT) 45Gy in 25 daily fractions with concurrent oral capecitabine (650mg/m² twice-daily 5 days/week) plus IV cetuximab (400mg/m² one week prior then weekly at 250mg/m² weeks 1-5) plus IV irinotecan (weekly at 60mg/m² weeks 1-4). Surgical resection was stipulated 8 weeks after CRT. EGFR pathway mutations were not assessed pre-treatment. DNA pyrosequencing was later performed on pre-treatment biopsies for mutation status of KRAS codons 12/13/61/146, NRAS codons 12/13/61, PIK3CA codons 542/545/546/1047, and the BRAF V600E hotspot.

Results

Between April 2009-October 2011 82 patients were recruited and 80 commenced RT. 76 patients underwent surgery with pathological complete response in 14(18%) and near-complete (microfoci) in 6(8%). 4 patients did not undergo surgery because of clinical complete response meaning 24(30%) had an excellent clinical or pathological response (ECPR). With median 26 month follow-up there were 3 pelvic failures, 15 metastatic failures and 13 deaths. 36-month progression-free survival (PFS, 21 events) was 65% (95%CI:51-76%) and overall survival 77%(95%CI:63-86%). Amongst the 24 ECPR patients 1(4%) progressed and none died. Amongst the 56 non-ECPR patients 20(36%) had a PFS event and 13(23%) died. Mutation status was available in 78 patients with KRAS mutation (34), BRAF(3), NRAS(3), PIK3CA(10) and pathway (any mutation)(45). There was no association between KRAS status (p=0.43) or pathway status (p=0.72) and ECPR. There was no association between KRAS status (36-month Restricted Mean Survival Time, p=0.99) or pathway status (unadjusted hazard ratio=0.79(95%CI:0.31-1.98; p=0.61)) and PFS.
Conclusion
The 30% ECPR rate and associated marked survival improvement were similar to our previous trial (RICE) using a similar regimen without cetuximab. EGFR pathway mutations did not predict histological response and were not prognostic for survival although follow-up and patient numbers are limited.

Acknowledgements
EXCITE was funded by the Cancer Research UK Bobby Moore Fund and educational grants from Merck Pharmaceuticals and Pfizer. Dr Gollins is a NISCHR AHSC Clinical Research Fellow. Dr West was funded by a Yorkshire Cancer Research Clinical Research Training Fellowship 2009-2011. Yorkshire Cancer Research funds Prof Quirke’s work programme.

References

Discussion
15.40 – 16.00
Parallel sessions

KEY TO THEMES:

D Diagnosis and therapy
E Epidemiology and prevention
I Information, patients and the public
S Survivorship and end-of-life care
C The cancer cell and model systems
T Tumour-specific research

D Application of nanotechnology to oncology

Room 11 Hosted by Katherine Vallis, Gray Institute for Radiation Oncology & Biology, Oxford, UK

16.20 – 16.25 Introduction by the host
16.25 – 16.50 Engineering of polymeric nanoparticles for medical applications
   Omid Farokhzad, Harvard Medical School, Boston, USA
16.50 – 17.15 Title TBC
   Kostas Kostaleros, The University of Manchester, UK
17.15 – 17.40 Nanosized agents for imaging guided drug delivery
   Simonetta Geninatti Crich, University of Torino, Italy
17.40 – 17.50 Discussion

C Autophagy, senescence and cell death

Room 3A Hosted by Daniel Murphy, University of Glasgow Institute of Cancer Sciences and Cancer Research UK Beatson Institute, UK

16.20 – 16.25 Introduction by the host
16.25 – 16.50 Title TBC
   Lars Zender, University Hospital Tuebingen, Germany
16.50 – 17.15 Mitochondrial dysfunction and autophagy in tumour progression and metastasis
   Kay Macleod, The University of Chicago, USA
17.15 – 17.40 DNA damage: An inherent flaw of apoptosis-mediated tumour suppression
   Stephen Tait, Cancer Research UK Beatson Institute and University of Glasgow, Glasgow, UK
17.40 – 17.50 Discussion

T Clinical application of translational research in breast cancer

Hall 1A Hosted by John Yarnold, The Institute of Cancer Research, London, UK

16.20 – 16.25 Introduction by the host
16.25 – 16.50 Translational metabolic treatments for breast cancer
   Adrian L Harris, University of Oxford, UK
16.50 – 17.15  Application of risk prediction to breast cancer prevention  
**Douglas Easton**, University of Cambridge, UK

17.15 – 17.40  Emerging new targeted therapies for advanced breast cancer  
**Nicholas Turner**, The Institute of Cancer Research, London, UK

17.40 – 17.50  Discussion

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**Immunotherapy of childhood cancer**

**Hall 1C**  
Hosted by **John Anderson**, Institute of Child Health, University College London, UK

16.20 – 16.25  Introduction by the host

16.25 – 16.30  CCLG prizewinner: RNA helicase A is essential for 1p36 gene KIF1Bb tumour suppression in neuroblastomas  
**Zhi Xiong Chen**, Ludwig Institute for Cancer Research, Solna, Sweden and National University of Singapore

16.30 – 16.55  T cell-based immunotherapy approaches for neuroblastoma  
**Karin Straathof**, Institute of Child Health, University College London, UK

16.55 – 17.20  Haploidentical transplantation as a platform for post-transplant immune therapy in childhood leukaemia  
**Rupert Handgretinger**, Children’s University Hospital, Tübingen, Germany

17.20 – 17.45  Natural killer T (NKT) cells as a novel platform for cancer immunotherapy with chimeric antigen receptors  
**Leonid S Metelitsa**, Baylor College of Medicine, Houston, USA

17.45 – 17.50  Discussion

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**Refractory breathlessness: Mechanisms and management**

**Room 4**  
Hosted by **Miriam Johnson**, Hull York Medical School, UK

16.20 – 16.25  Introduction by the host

16.25 – 16.50  Refractory breathlessness: Mechanisms and management  
**David Currow**, Flinders University, Adelaide, Australia

16.50 – 17.15  From biology to therapy: A translational approach to breathlessness  
**Richella Ryan**, University of Cambridge, UK

17.15 – 17.40  More than a clinical sign or symptom: The experience of breathlessness in advanced illness  
**Marjolein Gysels**, Cicely Saunders Institute, King’s College London, UK

17.40 – 17.50  Discussion

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**The ‘end game’ for tobacco control in the UK: Key priorities for science and policy to reduce smoking**

**Room 3B**  
Hosted by **Linda Bauld**, University of Stirling, UK

16.20 – 16.25  Introduction by the host
16.25 – 16.50  Challenges in realising the end game: Dealing with the tobacco industry  
Anna B Gilmore, University of Bath, UK

16.50 – 17.15  The international context for moving toward the ‘end game’ for tobacco control in the United Kingdom  
Geoffrey T Fong, University of Waterloo and Ontario Institute for Cancer Research, Canada

17.15 – 17.40  Smoking prevention: What we need to do  
Amanda Amos, University of Edinburgh, UK

17.40 – 17.50  Discussion

C The importance of knowing which way is up – the role of polarity in tumour suppression

Hall 1B  Hosted by Buzz Baum, University College London, UK

16.20 – 16.25  Introduction by the host

16.25 – 16.50  Functional characterisation of new molecular mechanisms involved in epithelial lumen morphogenesis  
Fernando Martin-Belmonte, Centro de Biología Molecular Severo Ochoa (CSIC-UAM), Madrid, Spain

16.50 – 17.15  Fat cadherins in the regulation of planar polarity, tissue growth and mitochondrial activity  
Helen McNeill, University of Toronto and Lunenfeld-Tanenbaum Institute of Mount Sinai Hospital, Toronto, Canada

17.15 – 17.40  Title TBC  
Alan Clarke, Cardiff University, UK

17.40 – 17.50  Discussion
Application of nanotechnology to oncology

Introduction
Katherine Vallis
Gray Institute for Radiation Oncology & Biology, Oxford, UK
16.20 – 16.25, Room 11

Nanotechnology is the science of the very small, on the scale of 1 to 100 nanometers. Many materials, including metals, polymers and carbon, acquire unique properties when engineered at the nanoscale, rendering them suitable for the development of nanomedicines and nanodiagnostics. Nanotechnology is being applied to oncology in several ways such as drug discovery, diagnostics, drug delivery, imaging and therapeutics. Targeted nanoparticle medicines are beginning to enter clinical trials with at least one, BIND-014, now advancing to Phase II. Current challenges, progress and prospects in cancer nanomedicine will be discussed in this session.

Engineering of polymeric nanoparticles for medical applications
Omid Farokhzad
Harvard Medical School, Boston, USA
16.25 – 16.50, Room 11

A variety of organic/inorganic materials are utilised to generate nanoparticles for drug delivery: Polymeric nanoparticles, dendrimers, nanoshells, liposomes, nucleic acid based nanoparticles, magnetic nanoparticles, and virus nanoparticles. Two most commonly used systems are polymeric nanoparticles and liposomes. Controlled release polymer technology impacts every branch of medicine: Ophthalmology, pulmonary, pain medicine, endocrinology, cardiology, orthopedics, immunology, neurology and dentistry, with several of these systems in clinical practice such as Atridox, Lupron Depot, Gliadel, Zoladex, Trolstart Depot, Risperidol Consta and Sandostatin LAR. The market of controlled release polymer systems extended beyond drug delivery is estimated at $100 billion and are used by over 100 million people a year. Polymeric nanoparticles deliver drugs in the optimum dosage over time, increasing the efficacy of the drug, maximising patient compliance and enhancing ability to use highly toxic, poorly soluble, or relatively unstable drugs. These systems can also be used to co-deliver two or more drugs for combination therapy. The surface engineering of these nanoparticles may yield them ‘stealth’ to prolong their residence in blood and the functionalisation of these particles with targeting ligands can differentially target their uptake by a subset of cells, increasing their specificity and efficacy. The successful clinical translation of therapeutic nanoparticles requires optimisation of many distinct parameters including: Variation in the composition of the carrier system, drug loading efficiency, surface hydrophilicity, surface charge, particle size, density of possible ligands for targeting, etc., resulting in a large number of potential variables for optimisation which is impractical to achieve using a low throughput approach. Recently, combinatorial approaches have been developed to precisely engineer nanoparticles and screen multiple nanoparticle characteristics simultaneously. Our goal is to review efforts in design and optimisation of polymeric nanoparticles for medical applications, which formed the foundation for the clinical translation of the first-in-human targeted and controlled-release nanoparticles (BIND-014) for cancer therapy.

Title TBC
Kostas Kostaleros
The University of Manchester, UK
16.50 – 17.15, Room 11
Nanosized agents for imaging guided drug delivery
Simonetta Geninatti Crich
University of Torino, Italy
17.15 – 17.40, Room 11

Targeting tumours with systems that combine delivery of drugs and imaging agents within a single formulation, represents one of the most important challenges for the treatment of cancer. In fact, the use of these nanotheranostic agents enable the non-invasive analysis of the pharmacokinetic and biodistribution of the nanomedicine formulation by measuring drug concentration in the target organ in real time, thereby adapting the therapeutic protocol to each patient individually, on the basis of biodistribution and efficacy monitoring. The recent development of more sensitive and high-resolution imaging techniques has catalysed exponentially the development of nanosized carriers for both imaging and therapeutic agents characterised by low toxicity and high biocompatibility. Due to its superb spatial resolution, magnetic resonance imaging (MRI) seems to be the technique of choice for monitoring drug delivery process and therapeutic output. Lipid-based nanosized particles have been proven as suitable carriers for the delivery of several therapeutic agents. Liposomes seem to be good candidates as the payload can be encapsulated in their internal aqueous cavity and/or intercalated in the phospholipid bilayer, thus allowing the transport of both hydrophilic and hydrophobic compounds. Clinical applications of liposomes in the delivery of anticancer agents for the treatment of different solid tumours are well established. A second class of exogenous particles herein considered is made up of poly(lactic-co-glycolic acid) (PLGA) polymeric nanoparticles that have the advantage of being biodegradable and very well tolerated. Finally, naturally occurring biological nanocarriers such as lipoproteins, apoferritin, or serum albumin are a good alternative for drug delivery with several advantages: i) their metabolic fate is well controlled; ii) they do not cause adverse immunological reactions; iii) they own defined biodistribution routes that may be exploited or modified according to the specificities of the therapeutic needs.

Discussion
17.40 – 17.50

Autophagy, senescence and cell death

Introduction
Daniel Murphy
University of Glasgow Institute of Cancer Sciences and Cancer Research UK Beatson Institute, UK
16.20 – 16.25, Room 3A

The session will cover some of the latest insights into intrinsic tumour suppressive mechanisms with an emphasis on in vivo models that illustrate both the role and therapeutic potential of engaging intrinsic tumour suppression to limit cancer. Speakers will be encouraged to combine recently published data with unpublished material relevant to the roles of autophagy, senescence and cell death in limiting cancer. The session is intended for an audience that is broadly familiar with but not necessarily specialist in the subject area, in particular students and postdocs considering future research and career trajectories.
Title TBC
Lars Zender
University Hospital Tuebingen, Germany
16.25 – 16.50, Room 3A

**Mitochondrial dysfunction and autophagy in tumour progression and metastasis**
Kay Macleod
The University of Chicago, USA
16.50 – 17.15, Room 3A

**DNA damage: An inherent flaw of apoptosis-mediated tumour suppression?**
Stephen Tait
Cancer Research UK Beatson Institute and University of Glasgow, UK
17.15 – 17.40, Room 3A

Mitochondria are often essential for apoptosis through a process termed mitochondrial outer membrane permeabilisation or MOMP. This event leads to robust activation of caspase proteases and rapid cell death. Originally regarded as an all-or-nothing event, we have previously found that some mitochondria can evade MOMP and allow cell survival when caspase activity is blocked. From this, we have been interested in whether the converse happens - can limited mitochondrial permeabilisation occur and, if so, what are its consequences? Utilising a microscopy-based approach, we find that novel, apoptosis-engaging chemotherapeutics – termed BH3-mimetics – can induce mitochondrial-permeabilisation in a limited cohort of mitochondria. However, rather than triggering cell death, limited mitochondrial permeabilisation leads to caspase-dependent, nuclear DNA damage. Significantly, we find that non-lethal engagement of MOMP can also trigger DNA damage in various tissues *in vivo*. Importantly, using a novel method to mimic ‘primed-to-die’ cancer cells, we find that BH3-only proteins themselves govern cellular sensitivity to MOMP induced DNA damage. These results argue that failure to properly execute mitochondrial-dependent apoptosis leads to DNA damage. Besides having important implications for apoptosis-mediated tumour suppression, our findings also provide the basis for new ways to manipulate apoptosis in a therapeutic context.

Discussion
17.40 – 17.50

**Clinical application of translational research in breast cancer**

**Introduction**
John Yarnold
The Institute of Cancer Research, London, UK
16.20 – 16.25, Hall 1A

The winners of the RCR Ross Prizes for the best poster and proffered paper presentations will be announced at the beginning of this session.

The session will take a step back from the direct clinical application of radiotherapy research and provide three internationally renowned speakers who will each address an area in which the biology of breast cancer is being explored and where there is optimism for translational research having a significant impact on clinical management.
Professor Adrian Harris will discuss changes in metabolic pathways in tumours, brought about by genetic lesions, and the sort of approaches that are being investigated to exploit these changes for treatment. This will be followed Professor Doug Easton revealing how deep gene sequencing might come in the future, influencing how breast cancer is managed and how personalised medicine may become a reality. Finally Dr Nicolas Turner will present data, and his thoughts on its application to oncology in the emerging new targeted therapies for patients with advanced breast cancer.

**Translational metabolic treatments for breast cancer**

Adrian Harris  
University of Oxford, UK  
16.25 – 16.50, Hall 1A

Changes in metabolism are the essential output of many genetic lesions in cancer and these are required for tumour growth, invasion and metastasis. Many key mutations in breast cancer, particularly PIK3A, but also HER2 oestrogen receptor, are heavily involved. Hypoxia biology represents a key area of metabolic difference between tumour cells and normal cells and besides the aerobic glycolysis frequently induced by oncogenes, further metabolic changes are induced by hypoxia. We have investigated these *in vitro* and *in vivo* and found recently that upregulation of glycogen metabolism and lipid uptake is essential for survival under hypoxia. Blockade of glycogen breakdown or synthesis or inhibition of key fatty acid binding proteins contributes to a marked reduction of tumour growth *in vivo*. These results are with knockdown of enzymes or binding proteins that are targetable and suggest another way of selective toxicity to breast cancer. Their expressions also differ by intrinsic phenotypes for breast cancer, for example, the glycogen pathway seems particularly important for triple receptor negative breast cancer survival. Induced essentiality represents another way of exploiting the metabolic differences by using antiangiogenic drugs to increase hypoxia and make tumour cells far more dependent on specific metabolic pathways. These include carbonic anhydrase-9 to regulate acid pH, as well as the enzyme pyruvic dehydrogenase kinase to switch off mitochondrial metabolism. In addition, new pathways of hypoxia signalling in window of opportunity studies with bevacizumab and metformin we have shown marked induction of many of these pathways in patients with breast cancer under hypoxia and modulation of glucose metabolism by metformin. It will be of substantial interest to combine these therapies. However, it is likely that there will be great heterogeneity in response and trying to define patients, which show the optimum response to bevacizumab metabolically or to metformin will help appropriate stratification in prospective studies.

**Application of risk prediction to breast cancer prevention**

Douglas Easton  
University of Cambridge, UK  
16.50 – 17.15, Hall 1A

There is growing interest in the idea that prevention strategies for breast cancer might be targeted on women at high risk. Until very recently, the main targeting was identification of carriers of BRCA1 and BRCA2 mutations in women with a strong family history, and use of prophylactic surgery and/or MRI screening. However, NICE guidelines for management of familial breast cancer have recently been updated to include prevention by tamoxifen/raloxifene in high risk women. In addition, there is increasing recognition that mammographic screening for breast cancer is only moderately effective, and might be more effective if targeted at women at increased risk.

In parallel, the ability to discriminate risk has improved markedly. Genome-wide SNP studies have identified close to 100 common genetic variants associated with breast cancer risk. While the risks associated with the common low-penetrance alleles are modest, these risks combine multiplicatively with each other and with *BRCA1* and *BRCA2*, and the combined
effect of the currently identified loci are sufficient to identify individuals at substantially higher and lower cancer risk. For example, 1% of the population have a risk that the more than 3 fold that in the general population, while 1% of the population have a risk that is less than 1/3 of the population risk. In addition, next generation sequencing has provided the potential for “panel” testing of a larger set of breast cancer associated genes. An effective targeted prevention programme will depend critically on being able to model combined effects of known genetic markers with mammographic density, family history and other important risk factors. We are developing our online risk prediction tool BOADICEA to provide such predictions. Equally, it will depend on the acceptability of risk-based management to individual women and to the population at large.

Emerging new targeted therapies for advanced breast cancer
Nicholas Turner
The Institute of Cancer Research, London, UK
17.15 – 17.40, Hall 1A

Discussion
17.40 – 17.50

Immunotherapy of childhood cancer

Introduction
John Anderson
Institute of Child Health, University College London, UK
16.20 – 16.25, Hall 1C

The three speakers will provide an overview, illustrated by their own research, on the use of gene and cellular therapies to target paediatric leukaemia and neuroblastoma. Therapeutic approaches will cover bi-specific antibodies, chimeric antigen receptors and NK/NKT therapies. The importance of targeting the tumour stroma for effective therapies will be described in the context of new insights of tumour/stroma interactions in these conditions.

CCLG prizewinner: RNA helicase A is essential for 1p36 gene KIF1Bb tumour suppression in neuroblastomas
Zhi Xiong Chen
Ludwig Institute for Cancer Research, Solna, Sweden and National University of Singapore
16.25 – 16.30, Hall 1C

Background
Developmental apoptosis of neuronal precursors is crucial in determining the final number of terminally differentiated cells. During neural development, cells undergo apoptosis as growth factors such as NGF becomes limiting. Abnormal NGF signaling or aberrant developmental apoptosis is implicated in pediatric nervous system tumors. Several genes act upon a developmental apoptotic pathway that is activated when NGF becomes limiting for neuronal progenitors and requires KIF1Bb. KIF1Bb is necessary and sufficient for neuronal apoptosis during NGF withdrawal. KIF1Bb maps to 1p36.2, a region that is frequently deleted in neural crest-derived tumors including neuroblastomas.

Method
Large-scale immunoprecipitation followed by mass spectrometry, cloning and mutagenesis studies, apoptosis assays, immunofluorescence, lentiviral expression or shRNA-based studies, siRNA silencing, RNA-SEQ, RT-PCR, immunohistochemistry, NGF withdrawal experiments, patient studies and mouse developmental models are the key methods used.

**Results**

We identified a transcriptional basis for KIF1Bb-induced apoptosis, which requires a RNA/DNA helicase known as RNA helicase A (DHX9). KIF1Bb interacts with DHX9 to promote translocation of cytoplasmic DHX9 into the nucleus, resulting in transcription of apoptotic XIAP-associated factor 1 (XAF1). Transcription-impaired or nuclear localization-impaired DHX9 is unable to potentiate KIF1Bb-induced cell death. Knockdown of DHX9 also protects from KIF1Bb-induced cell death whereas KIF1Bb negative mutants are unable to translocate cytoplasmic DHX9 into the nucleus. Furthermore, XAF1 silencing protects from KIF1Bb-induced apoptosis. In addition, a genome-wide shRNA library loss-of-function screen revealed a DHX9-interacting transcription factor ZIC2 that is deemed crucial for KIF1Bb-induced apoptosis. This further suggests that a DHX9-dependent transcriptional program initiated by KIF1Bb is required to induce apoptosis in neuroblastomas.

**Conclusion**

Recent literature strongly pointed to KIF1Bb as a bonafide tumor suppressor. Our findings provide a mechanistic understanding of this role, whereby KIF1Bb interacts with cytoplasmic DHX9 leading to its accumulation in the nucleus to initiate a unique transcriptional signature that includes apoptotic effectors such as XAF1.

**T cell-based immunotherapy approaches for neuroblastoma**

Karin Straathof  
University College London Institute of Child Health and Great Ormond Street Hospital, London, UK  
16.30 – 16.55, Hall 1C

Despite combination treatment approaches including surgery, radiotherapy and myeloablative chemotherapy, most children with high-risk neuroblastoma succumb to their disease. Survivors have considerable long-term morbidity due to intensive treatment. New treatment strategies are badly needed.

Chimeric antigen receptors (CARs) consist of the antigen recognising domain of an antibody linked to intracellular portions of T cell signalling receptors. Using retroviral vectors patient T cells can be engineered to express tumour-specific CARs. These CAR-engineered T-cells can penetrate a solid core of tumour, release inflammatory cytokines, lyse tumour cells, proliferate at sites of disease and persist *in vivo* for years.

Disialoganglioside GD2 provides an attractive target antigen for CAR T cell therapy: GD2 is expressed in virtually all neuroblastomas regardless of stage or site of disease while expression on normal tissue is limited. There is extensive experience targeting this antigen with monoclonal antibodies. In addition, adoptive T cell immunotherapy with a GD2-specific CAR has shown promise in a phase I study in refractory/relapsed neuroblastoma.

Since this phase I study, CAR design, vector technology and insight in optimal immunotherapy treatment regimens has evolved. Recently, with next generation CARs and combination with lymphodepletion, CD19-CAR T cell therapy has led to unprecedented responses in patients with chemotherapy resistant leukaemias.

Our preclinical and translational work of the next generation GD2-CAR T cell therapy study will be presented as well as strategies to further refine the specificity and improve the efficacy of this immunotherapy approach.
Haploidentical transplantation as a platform for post-transplant immune therapy in childhood leukaemia
Rupert Handgretinger
Children’s University Hospital, Tuebingen, Germany
16.55 – 17.20, Hall 1C

Allogeneic haematopoietic stem cell transplantation (HSCT) from a matched sibling (MSD) or a matched unrelated donor (MUD) is for a number of patients with malignant diseases the only curative approach. Over the time, the pool of potential donors has been increased by the addition of umbilical cord blood (UCB) and haploidentical donors (HAD). A major advantage of haploidentical transplantation is rapid donor identification and the continuous availability of the donor also after transplantation for further post-transplant cellular therapy strategies to avoid or to treat relapse of the underlying leukaemia. In order to prevent GvHD, in vitro graft-manipulation procedures to deplete T-lymphocytes from the graft are available and include CD34+ positive selection, CD3/CD19 depletion or the more recently described TcRαβ/CD19 depletion method. In addition, there is a choice of donor selection according to the donor’s killer immunoglobuline-like receptor (KIR) phenotype and NK alloreactive status.

The success of haploidentical stem cell transplantation depends, besides the eradication of the underlying malignant disease by the preparative regimen, to a large extent on the balance between the donor’s effector cells against the recipient’s tissues and their favourable reaction towards the malignant cells (graft-versus malignancy effect). Over the years, convincing evidence has accumulated that the transplanted donor innate immune system contributes to the eradication of residual malignant cells.

Therefore, cellular therapeutic strategies using donor-derived effector cells will play a more and more important role not only for the prevention or treatment of relapse of the underlying disease, but also for the prevention of severe and life-threatening side effects, such as therapy-refractory viral or fungal infections for the prevention and/or treatment of GvHD.

Natural killer T (NKT) cells as a novel platform for cancer immunotherapy with chimeric antigen receptors
Leonid S Metelitsa
Baylor College of Medicine, Houston, USA
17.20 – 17.45, Hall 1C

Advances in the design of chimeric antigen receptors (CARs) improved antitumour efficacy of redirected T cells in early-phase cancer clinical trials. However, high heterogeneity of CAR T cells limits their therapeutic potential. We proposed that CAR expression in Vα24-invariant NKT cells (NKTs) could build upon natural antitumour properties of these cells. Primary human NKTs were engineered to express a CAR against GD2 ganglioside (CAR.GD2), which is highly expressed in neuroblastoma and other solid tumours. We compared CAR.GD2 constructs that encoded CD3ζ chain alone (Gz), with CD28 (G28z), 4-1BB (GBBz), or CD28 and 4-1BB (G28BBz) co-stimulatory endodomains. CAR.GD2 expression rendered NKTs highly cytotoxic against neuroblastoma cells without affecting their native CD1d-restricted reactivity and ability to kill M2 macrophages. We also observed a striking Th1-like NKT-cell polarisation by 4-1BB-containing constructs that was dependent on EGR1 transcription factor. Compared with T and CAR.GD2 T cells, NKTs and CAR.GD2 NKTs better infiltrated neuroblastoma xenografts after adoptive transfer in humanised NOD/SCID/IL2Rγ(null) mice. Although CAR.GD2 NKTs and CAR.GD2 T cells had similar antitumour activity in this model, only the former spared recipients from graft-versus-host disease. These results establish the potential of NKTs to serve as a safe and effective cellular platform for antitumour CAR therapy either in autologous or allogeneic settings.
Participants will learn: i) the rationale for using NKT cells as a platform for CARs; ii) dual-specific cytotoxicity of CAR.
GD2 NKT cells against neuroblasts and tumour-associated macrophages; iii) Th1-polarising properties of CAR.GD2 constructs with a 4-1BB co-stimulatory endodomain; iv) the advantage of using NKT cells in allogeneic settings; v) current limitations of the NKT-based cellular platform.

Discussion
17.45 – 17.50

Refractory breathlessness: Mechanisms and management

Introduction
Miriam Johnson
Hull York Medical School, UK
16.20 – 16.25, Room 4

Chronic daily breathlessness, persistent despite optimal cancer treatment, is difficult for the patient, carer and clinician, resulting in a sense of therapeutic helplessness. However, there is a growing evidence base in our understanding of the impact and meaning of breathlessness for patients and carers, and for the effectiveness of pharmacological and non-pharmacological interventions.

This session will present key aspects of patient experience and the state of the art evidence base for pharmacological interventions (opioids, oxygen) and for complex non-pharmacological interventions. It will also highlight the importance of concurrent basic science research to elucidate mechanisms, thus identify further therapeutic targets.

Refractory breathlessness: Mechanisms and management

David Currow
Flinders University, Adelaide, Australia
16.25 – 16.50, Room 4

Chronic refractory breathlessness, defined as breathlessness that persists at rest or on minimal exertion despite optimising the treatment of any underlying causes that has persisted daily for more than three of the last six months, is highly prevalent across our community. A great deal of suffering results as a consequence of such breathlessness when it remains unrelieved.

The dominant paradigm would suggest that the mechanism is ultimately a mismatch between input into breathing, and the body’s ability to respond. Such a stimulus can be peripheral (restriction of chest movement, stretch receptors in lung parenchyma peripheral chemo-receptors) or central input (central chemo-receptors, cognitive input). Any factor that limits the ability to respond adequately to the insult will result in the subjective sensation of breathlessness.

The evidence for the symptomatic management of chronic refractory breathlessness has developed rapidly in the last decade. The gold-standard measure is either a visual analogue scale, a numerical rating scale, a Borg scale or a Likert scale. These need to be anchored for both the intensity (severity) and an affective component (unpleasantness) of breathlessness. The minimally clinically important difference in the reduction of chronic breathlessness on a visual analogue scale has been defined. A moderate response would be 11mm on a 100mm scale.

Systemic opioids have a strong evidence base to ensure the safe reduction in breathlessness with benefits maintained
over long periods of time. When adequately titrated, oral sustained release opioids are going to predictably help the majority of patients in whom they have started. For people already on opioids for other reasons the dose will need to be adjusted by 25% over baseline in order to achieve symptomatic benefit. Other medications being studied include nebulised opioids and nebulised frusemide. Non-pharmacological interventions include a number of evidence-based cognitive and physical interventions.

From biology to therapy: A translational approach to breathlessness
Richella Ryan
University of Cambridge, UK
16.50 – 17.15, Room 4

Breathlessness is a complex symptom arising from the interaction between physiological, psychological, social and environmental factors. There is a growing body of literature identifying the mechanisms underlying breathlessness genesis but much remains to be elucidated. A thorough understanding of the biological pathways involved is necessary in order to identify suitable therapeutic targets. A collaborative approach, involving basic scientists and clinical researchers, is likely to be necessary to achieve this.

My current work uses a collaborative translational approach, aiming to identify a new biological pathway in breathlessness which might be amenable to therapeutic manipulation. Due to the threatening nature of breathlessness, we hypothesise that the hypothalamic-pituitary-adrenal (HPA) axis (or stress system) is an important pathway in breathlessness processing and that psychological approaches to breathlessness management operate along this biological pathway. We plan to test this using salivary diurnal cortisol profiles as a biomarker.

In this presentation, I will summarise the known mechanisms underlying breathlessness, along with the current and postulated therapeutic targets associated with these mechanisms. I will then describe the gaps in our current knowledge, along with the challenges of translating our current scientific knowledge to clinical practice. Finally, as an example of a translational approach to breathlessness research, I will describe my current work which tests the hypothesis that the HPA axis is an important biological pathway in breathlessness processing.

References

More than a clinical sign or symptom: The experience of breathlessness in advanced illness
Marjolein Gysels
Cicely Saunders Institute, King’s College London, UK
17.15 – 17.40, Room 4

Breathlessness is a complex symptom to manage. Factors on multiple levels (physiological, psychological, social, environmental) interact, influencing perceptions of breathlessness, and possibly causing secondary physiological and behavioural responses. As a result, work on breathlessness, which initially focused exclusively on its clinical management, has more recently focused on the experience of breathlessness. Breathlessness causes considerable suffering for those experiencing it. It is associated with fear and anxiety and causes disability, loss of independence and social contact, and it forms a threat to people’s everyday quality of life. It is responsible for high levels of hospital admission and consequently hospital death. Patients who suffer from breathlessness are insufficiently supported to adequately manage this symptom on a daily basis and they are ill-prepared to cope with acute episodes. Within these limits of current care provision, a
minority of people do manage to maintain an acceptable level of well-being. The ingredients of the self-care which they
employ are instructive in finding successful strategies for relieving breathlessness. We will consider breathlessness as it is
experienced in cancer, where it tends to be a subordinate concern to the disease status, which influences its perception
and management. These findings have contributed to the development of the Breathlessness Support Service (BSS), which
has recently been evaluated, and we will present the patient’s view on the care received from this service.

Acknowledgements
We thank the team of the breathlessness programme and Cicely Saunders International whose funding supported the
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Benefit (PBPG-0808-17311). The views expressed are those of the author(s) and not necessarily those of the NHS, the
NIHR or the Department of Health.

Discussion
17.40 – 17.50

The ‘end game’ for tobacco control in the UK: Key priorities for
science and policy to reduce smoking

Introduction
Linda Bauld
University of Stirling, UK
16.20 – 16.25, Room 3B

Smoking prevalence in the UK has declined steadily in recent years but one in five adults still smoke. A current focus for
tobacco control science and policy is to work towards reducing prevalence to 5% or less in the coming decades.

This session will focus on new evidence about the key drivers for prevalence reduction including: Using price measures to
counteract the activities of the tobacco industry; addressing smuggling; the EU tobacco products directive and evidence
on health warnings and standardised packaging; point of sale interventions; and priorities for reducing the uptake of
smoking amongst young people. The session is aimed primarily at preventative medicine, behavioural science and public
health researchers, practitioners and policy makers.

Challenges in realising the end game: Dealing with the tobacco industry
Anna B Gilmore
University of Bath, UK
16.25 – 16.50, Room 3B

The transnational tobacco companies (TTCs) have been described as the vectors of the tobacco epidemic. Overwhelming
evidence that TTCs have “operated for years with the express intention of subverting the role of governments and of
WHO in implementing public health policies to combat the tobacco epidemic” led to the inclusion of Article 5.3 in the
WHO’s Framework Convention on Tobacco Control (FCTC). This Article requires that Parties to the treaty shall act to
protect their public health policies “from commercial and other vested interests of the tobacco industry in accordance
with national law” (http://www.who.int/fctc/guidelines/article_5_3.pdf).

Yet securing effective implementation of Article 5.3 is complex, in part because the TTCs have influenced the regulatory
framework through which public policies are assessed in a way that embeds corporate influence over policy making and favours corporate interests (see http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000202). Consequently TTCs remain highly influential. Moreover, although tobacco sales are falling in many countries and global sales are stagnating, TTC profits have been increasing, providing ample funding for their lobbying activities (see, for example, http://tobaccocontrol.bmj.com/content/21/2/119.abstract and http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2981493/).

This presentation will examine the difficulties of implementing effective public health policies when there is a powerful vested interest opposing them. It will do so using two contemporary case studies that build on earlier presentations in this session including TTC efforts to prevent the implementation of standardised tobacco packaging in the UK. It will go on to argue that these difficulties require novel solutions. In this light it will explore a variety of ‘end-game’ solutions that propose changes to the way tobacco is supplied or industry is regulated.

The international context for moving toward the ‘end game’ for tobacco control in the United Kingdom
Geoffrey T Fong
University of Waterloo and Ontario Institute for Cancer Research, Canada
16.50 – 17.15, Room 3B

As the concept of the ‘end game’ in tobacco control develops in the United Kingdom, assessing where the UK stands in comparison to other countries is a key step. This presentation will compare the UK’s position in tobacco use and in tobacco control policies to countries within the EU and throughout the world. I will present findings from the International Tobacco Control Policy Evaluation Project (ITC Project), an ongoing longitudinal cohort study being conducted in 22 countries, inhabited by over 50% of the world’s population and over 70% of the world’s tobacco users. The ITC Project is measuring the psychosocial and behavioural impact of tobacco control policies of the WHO Framework Convention on Tobacco Control (FCTC). Since 2002, the ITC Project in the UK has regularly assessed (close to annually) the impact of FCTC policies such as health warnings, price/tax, tobacco advertising, promotion, and sponsorship, smoke-free policies; my comparison will focus on packaging and labeling policies. I will also describe the model for product regulation of the US Food and Drug Administration (FDA), which was granted regulatory authority over tobacco products in 2009; the experiences of the FDA highlight the challenges and opportunities that will affect the efforts of the UK and other countries as they move toward developing a tobacco end game strategy.

Smoking prevention: What we need to do
Amanda Amos
University of Edinburgh, UK
17.15 – 17.40, Room 3B

There has been considerable success in reducing youth smoking in the UK over recent years, with smoking prevalence declining in adolescents and young adults. However, there are challenges in maintaining this decline in smoking initiation, particularly as smoking is increasingly concentrated among disadvantaged young people. This presentation will draw on current research to explore some of the key challenges that need to be addressed if we are to achieve a tobacco-free generation. This will include the findings of a recent systematic review on the evidence on effective action to reduce inequalities in youth smoking. It will argue that sustained action at the international, national and local levels is needed to continue to address the social norms around smoking in young people as well as to reduce young people’s access to tobacco and cigarettes. These include reducing children’s and young people’s exposure to positive images of
smoking through introducing standardised packaging (including tobacco products) and reducing positive media images (e.g. in films). These need to be supported by mass media and social marketing campaigns, targeted at disadvantaged groups, which continue to de-normalise smoking and maintain awareness about the risks. Decreasing the affordability of cigarettes through tax increases is central to reducing young people’s access to cigarettes. However, while under-age sales of cigarettes have declined, many young people still access them through proxy sales and social sources. Thus achieving a tobacco-free generation will also require more radical action including reducing the number of outlets selling cigarettes, as well as policy action outwith tobacco control to address the wider social determinants of inequalities and health.

**Discussion**

17.40 – 17.50

**The importance of knowing which way is up – the role of polarity in tumour suppression**

**Introduction**

**Buzz Baum**

University College London, UK

16.20 – 16.25, Hall 1B

This session will look at how polar cell organisation influences cell growth and death in the context of an epithelium. Each of the speakers will consider cell polarity from a different perspective, giving the audience a broad view of how epithelial polarity is generated and deregulated during cancer progression.

**Functional characterisation of new molecular mechanisms involved in epithelial lumen morphogenesis**

**Fernando Martín-Belmonte**

Centro de Biología Molecular Severo Ochoa (CSIC-UAM), Madrid, Spain

16.25 – 16.50, Hall 1B

Epithelial organs such as lungs, kidneys or the gut are made of cavities (alveoli, cysts or acini) and tubules (the nephron tubules). These components are lined by a monolayer of polarised cells, with an apical surface facing a lumen and a basolateral surface lining the cell-to-cell junctions and subjacent extracellular matrix (ECM). After polarisation, acquisition of a central lumen is the major event during epithelial organ development. Although epithelial cell polarisation has been widely studied, the molecular mechanisms that lead to lumen formation are poorly understood. MDCK cells plated in ECM (3D cultures) form spherical structures enclosing a central lumen (cysts) that resemble the epithelial organ structure, which is a powerful model for the study of lumen morphogenesis. In order to identify genes necessary for lumen morphogenesis we performed a transcriptional and functional screening. First, a microarray analysis was done to identify upregulated genes during lumen morphogenesis. Microarray data was validated by quantitative PCR, and finally a set of genes was selected to perform a functional analysis by siRNA silencing. We confirmed induction of 48 genes. The siRNA analysis indicated that 16 genes (33%) were required for normal lumen phenotype in 3D cultures. Furthermore, most of these genes are downregulated in epithelial cancers. The identification of these genes opens new ways for the understanding of the key molecular mechanisms that lead to the development of epithelial organs, and identify new
targets to treat epithelial tumours.

Supported by grants of the Human Frontiers Science Program (HFSP-CDA 00011/2009), Marie Curie (IRG-209382), MICINN (BFU2008-01916) and (CONSOLIDER CSD2009-00016) to FM-B; and JAE fellowships (MICINN) to AERF and SV; and a FPI fellowship (MICINN) to MG.

**Fat cadherins in the regulation of planar polarity, tissue growth and mitochondrial activity**

_Helen McNeill_

University of Toronto and Lunenfeld-Tanenbaum Institute of Mount Sinai Hospital, Toronto, Canada

16.50 – 17.15, Hall 1B

Fat cadherins are enormous cell adhesion molecules (560kDa) that planar polarity, tissue growth and spindle orientation during development. Fat cadherins are highly conserved from Drosophila to man. Fat cadherins do not bind to other Fat cadherins, but instead bind another large cadherin, Dachsous. Fat-Dachsous binding regulates activity of the Hippo kinase pathway, a well known and highly conserved growth regulatory pathway. Fat-Dachsous interactions also regulate planar polarity, and loss of planar polarity leads to cystic disease in mouse models. The mechanisms by which Fat regulates planar polarity and growth are still poorly understood. Using yeast two hybrid analysis, proteomic screens and genetic screens in Drosophila, we have recently identified an essential role for Fat cadherins in the regulation of mitochondrial activity. These studies indicate a direct role for Fat in control of cellular energy and ROS signalling in normal development, and suggest how loss of Fat function may contribute to human diseases.

**Title TBC**

_Alan Clarke_

Cardiff University, UK

17.15 – 17.40, Hall 1B

**Discussion**

17.40 – 17.50
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*Of those who replied to the follow-up client feedback questionnaire*
Programme at a glance

Prize winners announcement
09.00 – 09.10
Hall 1A  Gerard Evan, Chair of the 2013 Scientific Committee

Plenary lecture
Chaired by Irene Higginson, Cicely Saunders Institute, King’s College London, UK
09.10 – 09.50  Improving value in cancer care: The case for palliative medicine
  Hall 1A  R Sean Morrison, Hertzberg Palliative Care Institute, National Palliative Care Research Center, and Mount Sinai Medical Center, New York, USA

Parallel sessions
10.00 – 11.30  Cancer immunology and immunotherapy: Building on success
  Room 11  Hosted by Sergio Quezada, University College London Cancer Institute, UK
10.00 – 11.30  Cell migration in tumours
  Hall 1A  Hosted by Erik Sahai, Cancer Research UK London Research Institute, UK
10.00 – 11.30  Depression in advanced cancer – the orphan symptom?
  Hall 1C  Hosted by Mari Lloyd-Williams, University of Liverpool, UK
10.00 – 11.30  Humanising mouse models of cancer: How relevant are current models?
  Room 3B  Hosted by Owen Sansom, Cancer Research UK Beatson Institute, Glasgow, UK
10.00 – 11.30  Sarcoma – state of the art and science
  Room 12  Hosted by Penella Woll, Weston Park Hospital, Sheffield, UK
10.00 – 11.30  Supporting family carers: International evidence
  Hall 1B  Hosted by Sheila Payne, Lancaster University, UK
10.00 – 11.30  Using next-generation sequencing to transform clinical practice
  Room 3A  Hosted by Nazneen Rahman, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK

Networking and refreshment break
11.30 – 11.50  Registration area and galleria

Plenary lecture
Chaired by Harpal S Kumar, Chair of the National Cancer Research Institute
11.50 – 12.30  **Cancer predisposition: Past glories, future imperatives**  
Hall 1A  **Nazneen Rahman**, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK

**Closing remarks**  
12.30 – 12.40  **Harpal S Kumar**, Chair of the National Cancer Research Institute  
Hall 1A

**Networking and lunch (available to take away)**  
12.40 – 13.30  Registration area and galleria

**Satellite symposia**  
12.45 – 16.50  **Ensuring success in sample collection for clinical trials**  
Hall 1C  Hosted by **The Confederation of Cancer Biobanks**
14.00 – 17.00  **Making the transition to become an independent investigator**  
Room 4  Hosted by the **Experimental Cancer Medicines Centres Junior Investigator Network Group**
14.00 – 17.00  **2013 Neuroblastoma Research Symposium**  
Room 3A  Hosted by **The Neuroblastoma Society**
Improving value in cancer care: The case for palliative medicine
R Sean Morrison
Hertzberg Palliative Care Institute, National Palliative Care Research Center, and Mount Sinai Medical Center, New York, USA
09.10 – 09.50, Hall 1A

Modern palliative care, originally conceptualised in the 1960s as care for those with cancer at the end of life, has moved beyond this narrow scope to address the needs of all patients living with serious illness and their families from the time of diagnosis. Modern palliative care is focused on improving quality of life and providing an added layer of support to patients and families in the setting of a serious illness. It is provided at the same time as all other appropriate disease directed and curative treatments.

This plenary session will address three key objectives. First, I will review the needs of an aging society and the imperative for change in how health care is delivered. Second, I will discuss the evidence that demonstrates how modern palliative care improves value (defined as the ration of healthcare quality to cost) in healthcare. Specifically I will review the evidence examining the effect of palliative care on patients’ quality of life, patient and family satisfaction, and healthcare expenditures. This discussion will include data from a recently completed multisite study of the effect of palliative care on cancer care in the United States. Finally, this plenary discussion will describe new models of palliative care delivery in hospitals and community settings and review barriers and opportunities to further integration of palliative care within routine cancer care in both the USA and the UK.

Cancer predisposition genes: Past glories, future imperatives
Nazneen Rahman
The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK
11.50 – 12.30, Hall 1A

Cancer predisposition genes (CPGs) describe genes in which rare germline mutations result in clinically important increased risks of cancer. Over the last 30 years, more than 100 cancer predisposition genes have been identified, resulting in increased risks of more than 40 different cancers. These discoveries have provided important insights into genetic determinants of disease and mechanisms of oncogenesis. They have also led to substantial clinical benefits for cancer patients and their relatives. Faster, cheaper sequencing technologies are leading to a new wave of cancer predisposition gene discoveries and will allow gene testing to become available to many more individuals. In turn this is providing tremendous opportunities to improve cancer treatment and prevention. However, there are also potential pitfalls and risks of harm. Realising the promise of cancer predisposition genes will thus require careful implementation.
Parallel sessions

KEY TO THEMES:

D Diagnosis and therapy
E Epidemiology and prevention
I Information, patients and the public
S Survivorship and end-of-life care
C The cancer cell and model systems
T Tumour-specific research

D Cancer immunology and immunotherapy: Building on success
Room 11

Hosted by Sergio Quezada, University College London Cancer Institute, UK

10.00 – 10.05 Introduction by the host

10.05 – 10.30 Linking cancer exomes to cancer immunotherapy
Ton Schumacher, The Netherlands Cancer Institute, Amsterdam, The Netherlands

10.30 – 10.55 Chimeric antigen receptor modified T cells: Does receptor design and cell product composition matter?
Stanley Riddell, Fred Hutchinson Cancer Research Center and University of Washington, Seattle, USA

10.55 – 11.20 The FAP+ stromal cell establishes dominant immune suppression in an autochthonous model of pancreatic ductal adenocarcinoma
Douglas Fearon, University of Cambridge, UK

11.20 – 11.30 Discussion

C Cell migration in tumours

Hall 1A

Hosted by Erik Sahai, Cancer Research UK London Research Institute, UK

10.00 – 10.05 Introduction by the host

10.05 – 10.30 Intravital microscopy of cancer invasion, plasticity and integrin function: Targeting cancer resistance
Peter Friedl, Radboud University Nijmegen Medical Centre, The Netherlands and The University of Texas MD Anderson Cancer Center, Houston, USA

10.30 – 10.55 Cancer cell invasion in complex environments
Erik Sahai, Cancer Research UK London Research Institute, UK

10.55 – 11.20 Plasticity and physical mechanisms of cell migration in confinement
Ewa Paluch, University College London, UK

11.20 – 11.30 Discussion
**IS Depression in advanced cancer – the orphan symptom?**

*Hall 1C*  
Hosted by *Mari Lloyd-Williams*, University of Liverpool, UK  
10.00 – 10.05  
*Introduction by the host*  
10.05 – 10.30  
The assessment and classification of depression in advanced cancer  
*Alasdair G Rooney*, Western General Hospital, Edinburgh, UK  
10.30 – 10.55  
Advances in the treatment of depression in advanced cancer  
*Gary Rodin*, Princess Margaret Cancer Centre and University of Toronto, Canada  
10.55 – 11.20  
The impact of spiritual distress on psychological distress and depression  
*Mark Cobb*, Sheffield Teaching Hospitals, UK  
11.20 – 11.30  
Discussion

**C Humanising mouse models of cancer: How relevant are current models?**

*Room 3B*  
Hosted by *Owen Sansom*, Cancer Research UK Beatson Institute, Glasgow, UK  
10.00 – 10.05  
*Introduction by the host*  
10.05 – 10.30  
Using GEMM and PDX models of pancreatic cancer to identify new therapeutic opportunities in PDAC  
*Owen Sansom*, Cancer Research UK Beatson Institute, Glasgow, UK  
10.30 – 10.55  
A pre-clinical approach to the development of targeted therapies for paediatric cancers  
*Louis Chesler*, The Institute of Cancer Research, London, UK  
10.55 – 11.20  
The application of mouse models humanised for pathways controlling drug metabolism and disposition in anticancer drug development  
*C Roland Wolf*, University of Dundee, UK  
11.20 – 11.30  
Discussion

**T Sarcoma – state of the art and science**

*Room 12*  
Hosted by *Penella Woll*, Weston Park Hospital, Sheffield, UK  
10.00 – 10.05  
*Introduction by the host*  
10.05 – 10.30  
*Title TBC*  
*Jean-Yves Blay*, University Claude Bernard, Lyon, France  
10.30 – 10.55  
GIST molecular advances: Maximising response to targeted therapies  
*Jonathan A Fletcher*, Brigham and Women’s Hospital, Boston, USA  
10.55 – 11.20  
Developments in understanding the biology of bone sarcomas  
*Bass Hassan*, University of Oxford, UK  
11.20 – 11.30  
Discussion
Parallel sessions

15 Supporting family carers: International evidence
Hall 1B  Hosted by Sheila Payne, Lancaster University, UK
10.00 – 10.05  Introduction by the host
10.05 – 10.30  Supporting family carers: International evidence
  Gunn Grande, The University of Manchester, UK
10.30 – 10.55  Supporting family carers: Identifying differences between urban and rural care at the end of life in Canada
  Kevin Brazil, Queen’s University Belfast, UK
10.55 – 11.20  Supporting family carers: Outcome of caregiving in nationwide register-based Scandinavian studies
  Mai-Britt Guldin, Research Unit for General Practice, University of Aarhus, Denmark
11.20 – 11.30  Discussion

D Using next-generation sequencing to transform clinical practice
Room 3A  Hosted by Nazneen Rahman, The Institute of Cancer Research, London, UK
10.00 – 10.05  Introduction by the host
10.05 – 10.30  The Mainstreaming Cancer Genetics Programme: Integrating genetic testing into routine clinical practice
  Clare Turnbull, The Institute of Cancer Research, London, UK
10.30 – 10.55  The Heidelberg Centre for Personalized Oncology
  Christof von Kalle, National Center of Tumor Diseases, Heidelberg and German Cancer Research Center (DKFZ), Germany
10.55 – 11.20  The art and science of genomic characterisation – when and how to move from discovery to delivery
  Stephen Chanock, National Cancer Institute, NIH, DHHS, Bethesda, USA
11.20 – 11.30  Discussion
Cancer immunology and immunotherapy: Building on success

Introduction
Sergio Quezada
University College London Cancer Institute, UK
10.00 – 10.05, Room 11

The ability to mobilise one’s own immune system to target cancer has been recently proven effective in a series of high profile trials where targeting the T cell immune-inhibitory receptor CTLA-4 significantly increased survival of patients with late-stage melanoma. Nonetheless, and despite these promising results, positive and durable responses remain limited to a fraction of the treated patients, underscoring the need for further research in the field.

The goal of this session is to present cutting edge data expanding on the function and relevance of immune checkpoints such as CTLA-4, the recent and promising achievements of cellular therapies with chimeric antigen receptors, and the critical and limiting impact that the tumour microenvironment has on immunotherapy.

Linking cancer exomes to cancer immunotherapy
Ton Schumacher
The Netherlands Cancer Institute, Amsterdam, The Netherlands
10.05 – 10.30, Room 11

There is now very strong evidence that human cancers can be recognised and destroyed by T lymphocytes. As a first example, antibodies against T cell checkpoint molecules such as CTLA-4 and PD-1 have shown clear effects in clinical trials in melanoma and also other human tumours. As a second example, infusion of autologous ex vivo expanded tumour-infiltrating T cells has resulted in tumour regressions in phase I/II trials in a number of centers including the Netherlands Cancer Institute.

An important gap in our understanding of these therapies is which epitopes are the targets in T cell-mediated tumour destruction. Such knowledge would be of value to steer T cell reactivity specifically towards these antigens.

With the aim to dissect therapy-induced T cell activity in human cancer, we have developed technologies for high-throughput analysis of T cell responses. Here I will discuss recent data that demonstrate how the combination of these technologies with cancer exome sequencing can be used to uncover T cell reactivity against mutated proteins. From the data obtained, we conclude that the T cell based immune system commonly interacts with the consequences of DNA damage in human melanoma. The ability to describe patient-specific T cell responses against mutated antigens forms an important first step towards the development of personalised cancer immunotherapy.

Chimeric antigen receptor modified T cells: Does receptor design and cell product composition matter?
Stanley Riddell
Fred Hutchinson Cancer Research Center and University of Washington, Seattle, USA
10.30 – 10.55, Room 11

The adoptive transfer of T cells modified with synthetic receptors that selectively target molecules expressed on tumour cells is emerging as a potentially disruptive therapy for human B cell malignancies, and is likely to have applications in solid tumours. The design of these chimeric antigen receptors (CARs) has largely been empiric and needs to be tailored for individual target molecules, and perhaps for different malignancies. Our lab has focused on discovering and validating
novel targets for CAR T cell therapy on solid tumours that do not cause toxicity to normal tissues, and on optimising the

design of CARs that recognise these molecules to promote effective T cell signalling. Studies directed towards validating
ROR1 as a target for therapy of lung cancer and other solid tumours will be presented. A second focus of the lab is on
defining optimal compositions of CAR modified T cell products for therapy of CD19+ haematologic malignancies that
may provide for more reproducible in vivo efficacy. I will discuss the in vitro and animal model data that provide the

rationale for deriving therapeutic T cells from defined subsets and present the results in the initial patients enrolled on the
first clinical trial in which CD19 CAR T cells are manufactured from selected T cells and formulated in a defined product
composition.

The FAP+ stromal cell establishes dominant immune suppression in an autochthonous model
of pancreatic ductal adenocarcinoma
Douglas Fearon
University of Cambridge, UK
10.55 – 11.20, Room 11

Clinical studies examining the effects of monoclonal anti-CTLA-4, -PD-1 and -PD-L1 prove that molecular interventions
enhancing the function of T cells can reverse the growth of melanomas and certain adenocarcinomas. However, only
a minority of patients had objective responses, and none with pancreatic ductal adenocarcinoma (PDAC) responded.

One must conclude either that the majority of these cancers are inherently unresponsive to immunotherapies, or that an
additional process dominates over these T cell-directed therapies.

Human adenocarcinomas contain a fibroblast-like stromal cell identifiable by the membrane protein, fibroblast activation
protein-alpha (FAP). We reported in 2010 that conditionally depleting FAP+ cells from subcutaneous Lewis lung
carcinomas expressing ovalbumin (LL2/OVA) caused immune control of tumour growth. Depleting FAP+ cells did not
increase the number of peripheral OVA-specific CD8+ T cells, excluding an effect on T cell priming, so that relief from
immune suppression explained the phenomenon.

We have now characterised the FAP+ stromal cell in the KPC model of autochthonous PDA. Transcriptomic analyses show
that this FAP+ cell is identical to the carcinoma-associated fibroblast. As with the LL2/OVA tumour model, depleting
FAP+ cells from PDAC rapidly led to slowing of PDAC growth, which depended on a pre-existing spontaneous immune
response to cancer cells. Remarkably, the depletion of FAP+ cells also uncovered the anti-tumour effects of anti-CTLA-4
and anti-PD-L1, which were ineffective when given alone. Therefore, there is a hierarchy of tumoral immune suppression
in PDAC, with that mediated by the FAP+ stromal cell dominating over at least two that directly affect the function of T
cells. This conclusion implies that the full potential of clinical T cell immunotherapy of cancer may be achieved if immune
suppression by the FAP+ stromal cell can be interrupted.

Discussion
11.20 – 11.30
Cell migration in tumours

Introduction
Erik Sahai
Cancer Research UK London Research Institute, UK
10.00 – 10.05, Hall 1A

The migration of cancer cells into the surrounding tissue is an early event in metastasis. Cell migration is also crucial for the recruitment and function of the tumour stroma. A comprehensive understanding of cell migration in tumours therefore requires consideration of the extracellular matrix and the numerous paracrine interactions that occur in tumours. These topics will be explored. We believe that this session will be of great interest to those studying the tumour microenvironment, cell biology, and metastasis.

Intravital microscopy of cancer invasion, plasticity and integrin function: Targeting cancer resistance
Peter Friedl
Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands and The University of Texas MD Anderson Cancer Center, Houston, USA
10.05 – 10.30, Hall 1A

The tumour microenvironment contributes to cancer invasion, growth and survival and thereby impacts tumour responses to therapy. We here developed an intravital infrared multiphoton imaging model for the multi-parameter visualisation of collective cancer cell invasion, guidance by the tumour stroma, and short- and long-term resistance to experimental anti-cancer therapy. The data show for orthotopic fibrosarcoma and melanoma xenografts deep invasive growth driven by proliferation concurrent with collective invasion of multicellular strands along the normoxic perivascular stroma. Despite normoxia, perivascular invasion strands were resistant to high-dose hypofractionated irradiation (cumulative dose 20 to 20Gy) which otherwise was sufficient to induce regression of the tumour main mass. This invasion-associated radioresistance niche comprised several hundreds of cells in close proximity to stromal structures, including collagen, basement vascular and myofibre membranes, and was able to re-establish tumour growth and relapse, thus escaping other imaging modalities but in vivo microscopy. Using simultaneous inhibition of β1 and β3 integrins by RNA interference or combined anti-β1/αV integrin antibody treatment, however, proliferation arrest, anoikis induction was achieved, ablating both tumour lesion and the resistance niche. In conclusion, collective invasion is an important invasion mode in solid tumours into a microenvironmentally privileged survival niche which conveys radioresistance by integrin-dependent signals. These findings show how ‘dynamic in vivo cell biology’ identifies a key role for integrin-mediated signalling in mediating cross-talk (reciprocity) between the peri-tumour stroma and the tumour cells to mediate altered biology and response to therapy (plasticity).

Cancer cell invasion in complex environments
Erik Sahai
Cancer Research UK London Research Institute, UK
10.30 – 10.55, Hall 1A
Plasticity and physical mechanisms of cell migration in confinement
Ewa Paluch
University College London, UK
10.55 – 11.20, Location Hall 1A

Cell migration requires directional polarisation, usually achieved by the formation of a leading edge protrusion. Cells migrating in three-dimensional environments can form various protrusion types, including actin-filled lamellipodia and actomyosin contractility-driven blebs. The ability to switch between protrusion types has been proposed to facilitate motility in complex environments and to promote cancer dissemination. However, the minimal requirements and timescales of such plastic transitions are not known. Furthermore, while lamellipodia-driven migration has been extensively studied, the mechanisms underlying bleb-based migration are very poorly understood. We have been investigating these questions using Walker 256 carcinosarcoma cells, a rat tumour cell line that can form both blebs and lamellipodia during migration.

We showed that shifting the balance between actin protrusive activity and actomyosin contractility is sufficient to lead to immediate transitions between blebs and lamellipodia during cell migration. Such transitions could also be induced upon abrupt changes in the adhesiveness of the cell substrate.

We then asked how cell body translocation is achieved during bleb-based migration. We could show that this type of migration, common during tumour dissemination, does not require specific substrate adhesions as long as the cells are placed in a three-dimensional environment. Using molecular and biophysical approaches combined with microfluidic engineering and physical modelling we showed that in Walker carcinosarcoma cells, force transmission during locomotion does not require trans-membrane coupling to the substrate. Instead, these cells appear to use a friction-based mechanism, translating intracellular cortical flows into forward movement of the cell body. Such a mechanism of locomotion, which does not rely on specific cell-substrate adhesions, may be advantageous for cells crossing multiple tissues, as it does not require the expression of tissue-specific receptors.

Discussion
11.20 – 11.30

Depression in advanced cancer – the orphan symptom?

Introduction
Mari Lloyd-Williams
University of Liverpool, UK
10.00 – 10.05, Hall 1C

This session will include an overview of the assessment and management (both pharmacological and non-pharmacological) of depression in advanced metastatic disease. The session will be aimed at a multidisciplinary audience including patient and carer participants. Topics covered will be assessment, management, international classifications, spiritual distress and psychological distress and a vision for the future, including an overview of what can be learnt from mental health and primary care.
The assessment and classification of depression in advanced cancer
Alasdair G Rooney
Edinburgh Centre for Neuro-oncology, Western General Hospital, Edinburgh, UK
10.05 – 10.30, Hall 1C
Clinical depression adversely affects quality of life and is an independent predictor of mortality in patients with cancer. Identifying depression in the cancer setting can however be difficult.
This talk will highlight clinical and academic approaches to the assessment and classification of depression in advanced cancer. Topics include:
- How depression evolved as a psychiatric disorder in the 20th century.
- Particular difficulties diagnosing depression in the cancer setting.
- The frequency and correlates of depression in patients with advanced cancer.
- The utility of screening and case-finding tools for depression in cancer.
Consensus-based recommendations for diagnosing depression in cancer.

Advances in the treatment of depression in advanced cancer
Gary Rodin
Princess Margaret Cancer Centre and University of Toronto, Canada
10.30 – 10.55, Hall 1C
Depression is common in individuals with advanced disease and its prevalence rises toward the end of life. This symptom may be understood as a final common pathway of distress in this population related to the burden and meaning of disease, individual strengths and vulnerabilities, and the sense of connection to others. Typical antidepressant medications may be of value although their role in this context is relatively limited. Recent studies have begun to evaluate the benefit of shorter-acting medications in the treatment of depression in these patients. Psychotherapeutic intervention and control of physical symptoms is the mainstay of the treatment of depression in advanced disease. Evidence has begun to accumulate those semi-structured supportive-expressive interventions that allow reflective space and that help individuals find meaning address fears of dependency, vulnerability and suffering may help prevent and alleviate depressive symptoms in this population.

The impact of spiritual distress on psychological distress and depression
Mark Cobb
Sheffield Teaching Hospitals, UK
10.55 – 11.20, Hall 1C
Discussion
11.20 – 11.30
Humanising mouse models of cancer: How relevant are current models?

**Introduction**
Owen Sansom
Cancer Research UK Beatson Institute, Glasgow, UK
10.00 – 10.05, Room 3B

Genetically engineered mouse models (GEMMs) of cancer have been instrumental in studying cancer initiation, progression and evolution. There is great interest now in the mouse as a preclinical tool to identify new therapies and predict current regimes. However there are many differences between mouse and man; for example, drug metabolism and the immune system. This session will address current GEMM models to investigate drug treatments and the state of the art work being used to humanise mouse models.

Using GEMM and PDX models of pancreatic cancer to identify new therapeutic opportunities in PDAC
Owen Sansom
Cancer Research UK Beatson Institute, Glasgow, UK
10.05 – 10.30, Room 3B

Pancreatic cancer is a deadly disease where few therapies exist and limited improvements in standard of care have been made. I will give an overview of our current work using both genetically engineered mouse models (GEMM) that bear the mutations that occur in the human disease and patient derived xenografts (PDXs) to identify new therapeutic targets in pancreatic cancer.

Specifically I will give an overview of using these models to test the concepts of ‘exceptional responders’ and anti-metastatic approaches in surgically resectable disease. Furthermore I will discuss exciting new opportunities to target the pancreatic cancer microenvironment.

A pre-clinical approach to the development of targeted therapeutics for paediatric cancers
Louis Chesler
The Institute of Cancer Research, London, UK
10.30 – 10.55, Room 3B

Four common paediatric solid tumours (neuroblastoma, medulloblastoma, rhabdomyosarcoma and glioblastoma) account for the majority of deaths from relapsed, therapy refractory cancer in children. Cure rates have not increased in the last decade, despite the escalation of high-dose conventional chemotherapy and a corresponding increase in long-term toxicity. More effective and non-toxic therapeutics are urgently needed. One barrier delaying the development of novel oncogene-targeted therapeutics for children’s solid tumours is a lack of pre-clinical tumour models that fully recapitulate the clinical behaviour of these conditions.

Recent advances in systematic sequencing and profiling of paediatric tumour biopsies has identified disease-associated oncogenes and genomic alterations, which describe a proportion of poor-outcome tumours and can be modelled using genetically-engineered murine (GEM) systems. This presentation will address some of the major developments in GEM modelling for children’s solid tumours, such as the identification and tissue-specific overexpression of anaplastic lymphoma kinase (ALK) mutations, which account for a proportion of hereditary and acquired neuroblastomas, tissue-specific overexpression of MYCN, which provides models for high-risk neuroblastoma and medulloblastoma, and new opportunities for modelling of additional targets in other solid tumours.
Another significant roadblock to development of novel therapeutics is the inefficiency of GEM systems for this purpose, and the failure of additional pre-clinical systems such as subcutaneously implanted tumour xenografts to adequately predict clinical efficacy. The application of quantitative pre-clinical imaging technologies, such as ultrasound, magnetic resonance (MRI), computed tomography (CT) and other methodologies has helped to circumvent this issue, when such techniques are applied to pre-clinical trials in a formalised setting. Specific examples of imaging-driven pre-clinical trials will be discussed, both for the development of targeted oncotherapeutics and for assessment of therapeutic resistance to primary chemotherapies.

The application of mouse models humanised for pathways controlling drug metabolism and disposition in anticancer drug development

C Roland Wolf
University of Dundee, UK
10.55 – 11.20, Room 3B

Pharmacokinetic and pharmacodynamic relationships are of central importance in defining the efficacy of anticancer drugs. This is critically determined for many newly licensed and emerging anticancer drugs by their rate of metabolism by the cytochrome P450-dependent monooxygenase system. There is profound individual variability in the activity of these enzymes that can result either in lack of drug efficacy or in enhanced side effects. There are major species differences in these enzymes between small animals and man, both in P450 regulation and multiplicity. In order to develop models that more closely resemble the human situation we have humanised mice for the major cytochrome P450s involved in drug disposition together with the transcription factors that regulate their expression. We have created complex gene knockouts and humanisations where the major gene clusters have been deleted and substituted for their human counterparts. A mouse model has been created where the major enzymes involved in drug disposition in man are expressed in a single animal. These models have been applied to establish pharmacokinetic and pharmacodynamic relationships for tyrosine kinase and B-Raf inhibitors in the treatment of cancer. These data will be described in this presentation.

Thank you for to all who contributed to this work:

C Roland Wolf¹, Nico Scheer², Anje Rode¹, Stephanie L Sharp¹, Kenneth AZ MacLeod¹, Zoe Riches¹, Michael MJ McMahon¹, Yury Kapelyukh¹, Lesley M McLaughlin¹ and Colin J Henderson¹

¹University of Dundee Medical Research Institute, Division of Cancer Research, Jacqui Wood Cancer Centre, Ninewells Hospital and Medical School, Dundee, DD1 9SY, UK
²TaconicArtemis, Neurather Ring 1, 51063 Cologne, Germany

Discussion
11.20 – 11.30
Sarcoma – state of the art and science

Introduction
Penella Woll
Weston Park Hospital, Sheffield, UK
10.00 – 10.05, Room 12

Sarcomas are a rare and heterogeneous tumour group that can affect patients of all ages, and all sites in the body. Recent developments in molecular biology have led these tumours to be redefined, and led to the introduction of novel approaches to treatment. The speakers will review the impact of these developments in three distinct areas: gastrointestinal stromal tumours (GIST), soft tissue, and bone sarcomas. Their talks will span from tumour biology to patient management. The session will have broad appeal to scientists, pathologists, surgeons and oncologists.

Title TBC
Jean-Yves Blay
University Claude Bernard Lyon, France
10.05 – 10.30, Room 12

GIST molecular advances: Maximising response to targeted therapies
Jonathan A Fletcher
Brigham and Women’s Hospital, Boston, USA
10.30 – 10.55, Room 12

Developments in understanding the biology of bone sarcomas
Bass Hassan
University of Oxford, UK
10.55 – 11.20, Room 12

Primary bone sarcomas are rare tumours with a wide spectrum of clinical and biological behaviour. They range from highly aggressive Ewing sarcoma and osteosarcoma that present in young patients, to often slower growing chondrosarcoma that can transform to higher grade forms in older adults. Curative approaches to locally aggressive tumours such as giant cell tumours of bone, and even rarer types of bone tumours are also challenging to specialist teams. As with many other tumours, histological classification is now being combined with molecular classification of disease subtypes, and in particular with somatic genome based diagnostics. Basic research has progressed quickly because of the new information provided by next generation sequencing technologies and experimental model systems, and these are now beginning to shape the next generation of clinical studies. Ultimately, predictive correlation will enhance the impetus towards improved diagnosis, target validation and stratified or personalised treatment options. Translation into practice will require new approaches to clinical trial design that will exploit the strong international collaboration between researchers in all disciplines that has developed within the field. Whilst large scale clinical trials have standardised care worldwide, I will review the emerging advances in basic biology and translational research studies that will underpin the next wave of hypothesis and treatment advances.

Discussion
11.20 – 11.30
Supporting family carers: International evidence

Introduction
Sheila Payne
Lancaster University, UK
10.00 – 10.05, Hall 1B

This session aims to highlight the important topic of how best to support lay people (family, friends and significant others; hereafter called ‘family carers’) who provide care to patients during the cancer trajectory. It is widely recognised that these people have an essential role in providing physical care, emotional and social support, financial resources, advocacy and anticipatory care, and in negotiating and coordinating care during all phases of cancer. The presence of family carers who are able and willing to provide care is essential to facilitate patient choices, such as place of care. It is a challenging and demanding role.

Supporting family carers: International evidence
Gunn Grande
The University of Manchester, UK
10.05 – 10.30, Hall 1B

This talk considers ‘family’ in its broadest sense and uses the NICE (2004) definition of carers as ‘lay people in a close supportive role who share in the illness experience of the patient and undertake vital care work and emotion management’. This presentation will mainly focus on supporting family carers towards the end of the patient’s life, but most issues will span the patient’s disease trajectory. Carers make a substantial contribution to the economy, and carers play a vital role in providing psychological and physical support for patients, negotiating and coordinating their care, and in enabling patients to remain at home towards the end of life. However, many come to this role without any preparation, and care giving can have substantial psychological, physical, social and financial impact on carers. Whilst some demographic and clinical factors may help predict carers ‘at risk’ of adverse impacts, psychological variables such as self-esteem and preparedness may be more important and amenable to intervention. When trying to support carers, we face several challenges and gaps in our knowledge. Overall there has been relatively little research on interventions for caregivers and their effectiveness. Furthermore, research to date has given little attention to potential rewards of care giving and how we may nurture these aspects. Carers occupy an ambiguous role both as providers of support and as potential clients requiring support in their own right, and we need to negotiate and address both to provide effective support. Finally, care gving is a dynamic process that evolves over time, and we require more longitudinal research and better theoretical models to understand this process. In the developed world demographic changes pose likely future challenges where more patients with complex care needs are looked after by fewer carers who face increasing care giver burdens.
Supporting family carers: Identifying differences between urban and rural care at the end of life in Canada
Kevin Brazil
Queen’s University Belfast, UK
10.30 – 10.55, Hall 1B
Approximately 20% of North Americans and 25% of Europeans are identified as living in rural areas. The provision of palliative care in rural areas has generated interest in several countries. This attention is, in part due to the view that palliative care is now recognized as a basic human right and that individuals prefer to be treated in their own communities and die in their own homes. The issue of geographic inequity in access to palliative care is sharpened with the knowledge of an expected rise of an aging population that will amplify the need for palliative care.

The unique challenges associated with the provision of health care to terminally ill patients in rural settings suggests informal carers assume a greater role than their urban counterparts. Unfortunately little is know about the experience of informal caregiving in rural regions at the end of life. Considering geographic location as place of care this presentation will provide an overview on how the family carer experience is understood in Canada. Key findings from a recently completed study will elucidate the influence of location as place of care. Aspects of the family carer experience that will be reviewed will include; identified support needs, the experience of burden in caregiving, the role of social support, perception of access to formal care; and, the pattern of formal care used by the palliative family member. Implications for policy and service development will be identified.

Supporting family carers: Outcome of caregiving in nationwide register-based Scandinavian studies
Mai-Britt Guldin
Research Unit for General Practice, University of Aarhus, Denmark
10.55 – 11.20, Hall 1B
Objective
Caregiving has been shown to be both rewarding and demanding. In Denmark and the Scandinavian countries, family carers are increasingly seen as an important resource in end-of-life care. Previous studies have found an increased risk of healthcare utilisation and psychological distress in family caregivers, e.g. anxiety, depression and complicated grief, placing caregivers in a vulnerable position. A number of factors have been shown to influence development of distress in family caregivers. This presentation aims to provide information on current studies of caregiving in Scandinavia with a focus on nationwide register-based studies.

Methods
The studies were designed as nationwide cohort studies or case-control studies combined with questionnaire data. The study populations were identified through Danish or Swedish healthcare registries to investigate the effects of caregiving.

Results
In all studies, caregiving resulted in an increased risk of psychological and even physiological morbidity among carers during the illness and after the loss of a loved one. Psychological distress was mostly measured as depression and anxiety. In one large-scale study, patterns of healthcare utilisation were investigated to reveal the impact of caregiving on the entire healthcare system.
Parallel session abstracts

Conclusions
The results of the studies indicate a need for improved awareness of the impact of caregiving. This presentation will provide valuable information on the association of caregiving and healthcare utilisation as well as psychological distress in family caregivers from register-based nationwide Scandinavian studies. Future perspectives include targeted support for family caregivers to help prevent adverse effects of caregiving.

Discussion
11.20 – 11.30

Using next-generation sequencing to transform clinical practice

Introduction
Nazneen Rahman
The Institute of Cancer Research, London, UK
10.00 – 10.05, Room 3A

Next generation sequencing (NGS) technologies make the routine testing of both genetic predisposition to cancer and tumour-specific mutations a realistic aspiration for cancer care. Information about acquired and intrinsic genetic variation can inform diagnosis, classification and treatment, as well as risks of recurrence, secondary cancers and cancer risks in family members. Fundamental changes in health service infrastructure, workforce training, and clinician and public perceptions are required for the full promise to be realised. This session presents perspectives from the UK, Europe and the US regarding the processes, benefits and complexities of integrating somatic and germline genetic testing into routine oncological care.

The Mainstreaming Cancer Genetics Programme: Integrating genetic testing into routine clinical
Clare Turnbull
The Institute of Cancer Research, London, UK
10.05 – 10.30, Room 3A

Genetic testing of cancer predisposition genes is one of the major activities of clinical genetics. Currently, nearly 100 genes associated with predisposition to cancer are known, but in most countries testing is very restricted with respect to the number of genes and the number of people tested. The value of genetic testing in individuals with cancer is underappreciated; it provides important information with respect to the cause and optimal treatment of the current cancer, and the risk and optimal management of future cancer. Moreover, testing cancer patients followed by cascade testing of mutation carriers is an effective and efficient way of identifying unaffected mutation carriers in whom screening and risk-reducing strategies can be deployed. The Mainstreaming Cancer Genetics (MCG) Programme is a UK national cross-disciplinary initiative to develop the next generation sequencing (NGS) assays, analytical and interpretive pipelines, clinical infrastructure, training, ethical and evaluation processes required for routine genetic testing to be integrated into cancer patient care. In collaboration with Illumina, we have developed a NGS panel targeting 97 cancer predisposition genes with >1500 probes (called the TruSight cancer panel) and have completed detailed evaluation of performance, sensitivity and specificity under different levels of multiplexing, coverage and throughput. We are using bespoke analytical pipelines developed for high-throughput clinical diagnostic data analysis (called GAMA) and clinical interpretation (called
CIGMA). We are implementing a new mixed-model of cancer gene testing whereby consent for medical testing (i.e. in cancer patients) is undertaken by oncologists, with only the mutation carriers seen by geneticists. Predictive testing (i.e. in unaffected individuals) will continue to be undertaken in genetics. We have developed protocols and e-learning modules to deliver the required training for oncologists. We hope this model will allow throughput of testing to greatly increase, whilst retaining input and support from genetics, where it is required. We are currently piloting the new model in ovarian and breast cancer patients at the Royal Marsden Hospital.

www.mcgprogramme.com

The Heidelberg Center for Personalized Oncology
Christof von Kalle
National Center for Tumor Diseases and German Cancer Research Center (DKFZ), Heidelberg, Germany
10.30 – 10.55, Room 3A

Next-generation sequencing (NGS) has transformed genomic research by entering an era in which the cost of clinical whole-genome and targeted sequencing tests is no longer prohibitive to their application. New opportunities for translating high-throughput functional genomics into clinical practices have been afforded. By combining forces between genomics, systems biology and translation, the German Cancer Research Center has begun to form an internationally leading center for personalised oncology. The mid- to long-term goal of this center is to develop a programme for personalised oncology that will readily translate latest research and technologies from the field of functional genomics and systems biology into clinical practice. Clinical use of NGS technologies will enable the identification of causative mutations for rare genetic disorders through whole-genome or targeted genome resequencing, rapid pathogen screening and cancer diagnosis along with the identification of appropriate therapy. We have set up a technology platform that integrates the next-generation sequencing platform for the analysis of whole genomes, methylomes and transcriptomes with a bioinformatics platform that hosts Germany’s largest data facility in life sciences together with the genome data analysis group. The genomic sequencing oriented platforms will be complemented by a mass spectrometry-based proteomics platform. For detailed mechanistic studies of deregulated pathways in vivo we will establish a next-generation microscopy imaging platform. As a principal portal of entry for all oncology patients into the Heidelberg University Medical School, NCT provides optimal interdisciplinary oncology and allows the rapid transfer of scientific knowledge into clinical applications. Routine clinical use of NGS technologies is appealing, but mandates high accuracy, simple assays, flexible throughput, short run times and most importantly, easy data analysis as well as interpretation; all features we are working on to optimise, to reach the NCT Precision Oncology Program (NCT-POP) ultimate goal of providing comprehensive high-throughput molecular analysis for every patient at the center by 2015.

The art and science of genomic characterisation – when and how to move from discovery to delivery
Stephen Chanock
National Cancer Institute, NIH, DHHS, Bethesda, USA
10.55 – 11.20, Room 3A

Discussion
11.20 – 11.30
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Email: customercare_uk@agilent.com  
Phone: +44 (0)845 712 5292  
5500 Lakeside, Cheadle Royal Business Park, Cheadle, Cheshire, SK8 3GR, UK

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**AICR (Association for International Cancer Research)**  
Exhibition Stand Unit: 47

A relatively young charity, AICR (www.aicr.org.uk) has a well established reputation for funding top quality research. World class scientists acknowledge the importance of receiving a grant from the Scottish charity, which aims to fund the best research, wherever in the world that is taking place. 177 such projects are active now.

**www.aicr.org.uk**

Contact: Debbie Wheelans, Grants Manager  
Email: debbie.wheelans@aicr.org.uk  
Phone: +44 (0)1334 477 910  
Fax: +44 (0)1334 478 667  
Madras House, South Street, St Andrews, Fife KY16 9EH, UK
American Peptide Company Europe
Exhibition Stand Unit: 58

American Peptide Company offers comprehensive selections of pre-manufactured catalogue peptides, custom synthesis, and GMP peptide Active Pharmaceutical Ingredients. Our California based manufacturing facilities offer synthesis under non GMP and cGMP conditions, and our Total Peptide Management services support clients in the drug development process from pre-clinical through to commercial stage.

www.americanpeptide.com

Contact: Stewart Hamilton, Director Sales and Marketing Europe
Email: stewart@americanpeptide.com
Phone: +44 (0)1629 582 441 / +44 (0)7515 151 312
43 Lime Tree Road, Matlock, DE4 3EJ, UK

Amgen Oncology
Exhibition Stand Unit: M2

Amgen discovers, develops, manufactures, and delivers innovative human therapeutics. A biotechnology pioneer since 1980, Amgen was one of the first companies to realize the new science’s promise by bringing safe, effective medicines from lab to manufacturing plant to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, bone disease, and other serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people’s lives. For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

www.amgen.com

Contact: Jodie Ellis, Medical Communications Manager
Email: jodiee@amgen.com
Phone: +44 (0)1223 436 711
240 Cambridge Science Park, Milton Road, Cambridge, CB4 0WD, UK
AMSBIO
Exhibition Stand Unit: 56

Founded in 1987, AMSBIO provides cutting-edge life science technology products and services, which accelerate development in the medical, nutrition, cosmetics and energy industries. The AMSBIO range includes specialist antibodies, peptides and recombinant proteins as well as solutions for studying cell motility, migration, invasion and proliferation. Key research areas for these products include: Oncology, Regenerative Medicine, Environmental Analysis, Cytotoxicity Screening, Glycomics and Stem Cell Biology.

www.amsbio.com

Contact: Alex Sim, Managing Director
Email: info@amsbio.com
Phone: +44 (0)1235 828 200    Fax: +44 (0)1235 820 482
184 Milton Park, Abingdon, OX14 4SE, UK

Barts Cancer Institute
Exhibition Stand Unit: 52 & 53

The BCI’s ethos is interdisciplinary and integrated, focusing on haematology, pancreatic, lung, women’s and men’s cancer, with comprehensive tissue banks, now extended to include pancreatic and metastatic tissues. Key strengths include clinical trials, and basic science in genomics, cell signalling and tumour-stromal interactions. Cancer and Ageing is a new initiative.

www.bci.qmul.ac.uk

Contact: Katie Hale
Email: k.hale@qmul.ac.uk
Phone: +44 (0)20 7882 3503    Fax: +44 (0)20 7882 3888
Old Anatomy Building, Charterhouse Square, London EC1M 6BQ, UK
Bioline Reagents Ltd
Exhibition Stand Unit: 44

Bioline develops and manufactures a wide range of specialized bio-research reagents that simplify, accelerate and improve life sciences research. Our mission is to provide customers with products which are fast and easy to use, developed by scientists who understand our customer’s needs, so they can focus on their scientific goals.

www.bioline.com

Contact: Agnes Szubert, UK Sales and Marketing Coordinator
Email: info@bioline.com
Phone: +44 (0)20 8830 5300 Fax: +44 (0)20 8452 2822
16 The Edge Business Centre, Humber Road, London, NW2 6EW, UK

BMJ
Exhibition Stand Unit: 25

BMJ advances healthcare worldwide by sharing the latest and best knowledge and expertise. Our products and services support all healthcare providers, from individual clinicians to major organisations. We are committed to improving patient experiences and outcomes, promoting better value health services and assisting the continuing professional development of clinicians everywhere.

BMJ Open (bmjopen.com) is an open access international general medical journal, dedicated to publishing medical research from all disciplines and therapeutic areas, including oncology. The journal publishes all research study types, from study protocols to phase I trials and meta-analyses. Visit stand #25 to find out more about our oncology collection.

www.bmj.com/company

Contact: Kylie Petitt, Marketing Co-ordinator
Email: kpetitt@bmj.com
Phone: +44 (0)20 7383 6706
BMA House, Tavistock Square, London, WC1H 9JR, UK
Breast Cancer Campaign
Exhibition Stand Unit: 68

We fund world-class breast cancer research with the greatest potential to save and improve lives, bringing together the brightest minds to share knowledge and produce better, quicker results. We do this because we passionately believe we owe it to every woman affected by breast cancer to explore every avenue to overcome and outlive this disease — in our lifetime.

www.breastcancercampaign.org

Contact: Phyllis Quinn, Research Grants Manager
Email: pquinn@breastcancercampaign.org
Phone: +44 (0)20 7749 0893
Clifton Centre, 110 Clifton Street, London, EC2A 4HT, UK

Bristol-Myers Squibb
Exhibition Stand Unit: 63

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail against serious diseases. Around the world, our medicines are helping millions of patients in their fight against such diseases as cancer, cardiovascular disease, diabetes, hepatitis B, HIV/AIDS, psychiatric disorders and rheumatoid arthritis.

Contact: Christina Cockley, Medical Education Manager, Oncology
Email: christina.cockley@bms.com
Phone: +44 (0)7753 976 705   Fax: +44 (0)1895 523 547
Uxbridge Business Park, Sanderson Road, Uxbridge, UB8 1DH, UK
British Association for Cancer Research (BACR)
Exhibition Stand Unit: 87

The aim of the BACR is to promote the advance of research in relation to all aspects of cancer, both laboratory and clinical, and to encourage the exchange of information. Its functions are to organise scientific meetings and workshops; fund exchanges between laboratories to encourage knowledge transfer; provide opportunities for senior investigators to undergo further training; and to provide for junior investigators and research students the opportunity to present their work at meetings and conferences.

www.bacr.org.uk

Contact: Janet Alexander, Administrative Secretary
Email: bacr@leeds.ac.uk
Phone: +44 (0)113 206 5611 Fax: +44 (0)113 206 5611
Leeds Institute of Cancer and Pathology (LICAP), Cancer Research Building, St James’s University Hospital, Beckett Street, Leeds, LS9 7TF, UK

CaCTUS (Cancer Clinical Trials Unit Scotland)
Exhibition Stand Unit: 57

Cancer Clinical Trials Unit Scotland (CaCTUS) is a partnership between the Cancer Research UK Clinical Trials Unit in Glasgow and the NHS ISD Cancer Clinical Trials Team in Edinburgh. CaCTUS is an accredited National Cancer Research Institute (NCRI) CTU and is a registered UK Clinical Research Collaboration (UKCRC) CTU.

CaCTUS offers support for all aspects of management of cancer clinical trials and is committed to working with Investigators to develop and manage new cancer clinical trials.

www.cactusonline.org.uk

Contact: Judith Dixon, Project Manager
Email: judith.dixon@glasgow.ac.uk
Phone: +44 (0)141 301 7540 Fax: +44 (0)141 301 7244
CR-UK Clinical Trials Unit, Level 0, Beatson West of Scotland Cancer Centre, 1053 Great Western Road, Glasgow, G12 0YN, UK
Cancer Research Technology Ltd
Exhibition Stand Unit: 59

Cancer Research Technology is owned by Cancer Research UK, the world’s largest charitable funder of cancer research. We’re dedicated to advancing discoveries to beat cancer by translating promising scientific research into attractive commercial propositions. We provide services to oncology institutions worldwide, as well as operating our own drug discovery laboratories.

www.cancertechnology.com

Contact: Karen Worthing, Marketing Manager
Email: enquiries@cancertechnology.com
Phone: +44 (0)20 3469 6300  Fax: +44 (0)20 3014 8633
Angel Building, 407 St John Street, London, EC1V 4AD, UK

Cancer Research UK
Exhibition Stand Unit: S2

Cancer Research UK is the largest single funder of cancer research in the UK. We support research into all aspects of cancer through the work of more than 4,000 scientists, doctors and nurses. Visit our stand to find out more about the funding and support we provide and other ways you can get involved with us.

www.cruk.org

Contact: Karen Walshe, Research Brand and Communications Lead
Email: karen.walshe@cancer.org.uk
Phone: +44 (0)20 7242 0200
Angel Building, 407 St John Street, London, EC1V 4AD, UK
Cancer Research UK Centre, Southampton – CTU and ECMC

Exhibition Stand Unit: M3

Cancer Research UK Centre in Southampton is a partnership between CRUK, University of Southampton and University Hospital Southampton NHS Foundation Trust. Working alongside the CRUK Centre, are University of Southampton Clinical Trials Unit, which delivers large multi-centre trials; and the Experimental Cancer Medicine Centre, uniting laboratory and clinical research teams.

www.ctu.soton.ac.uk
www.southampton.ac.uk/cruk
www.ecmcnetwork.org/network-centres/southampton/

Contact: Jo Musgrove, Quality and Regulatory Manager
Email: ctu@soton.ac.uk
Phone: +44 (0)2380 795 154 Fax: +44 (0)844 744 0621
University of Southampton Clinical Trials Unit, Mailpoint131, Southampton General Hospital, Tremona Road, Southampton, Hampshire, SO16 6YD, UK

Caris Life Sciences

Exhibition Stand Unit: 32

Caris Life Sciences, a leading biosciences company, provides the world’s foremost evidence-guided tumour profiling service, Caris Molecular Intelligence. Our service, for solid tumours, matches each patient’s biomarker test results, with drug associations described in the clinical literature. Our informative reports are intended to help the clinician decide which therapies may be effective or ineffective, for each individual patient.

www.carislifesciences.eu

Contact: Arlene Campbell
Email: EUCustomerService@carislsl.com
Phone: +44 (0)121 533 5300 Fax: +44 (0)121 533 5301
St Jakobsstrasse 199, CH 40542 Basel, Switzerland
Celgene Ltd  
Exhibition Stand Unit: 49

Celgene is a global biopharmaceutical company committed to improving the lives of patients worldwide. Celgene seeks to deliver truly innovative and life-changing medicines for patients. The company focuses on the discovery, development and commercialisation of products for the treatment of cancer and other severe, immunological, inflammatory conditions.

Celgene’s haematological cancer portfolio includes products for the treatment of multiple myeloma and the only drug approved in Europe for the treatment of myelodysplastic syndromes.

www.celgene.co.uk

Date of preparation: January 2013
UK-CELG130004

Charles River  
Exhibition Stand Unit: 33

Charles River helps researchers identify promising anticancer compounds and optimize lead candidates. We offer a robust portfolio of immunodeficient and genetically engineered animal models and have experience testing anticancer agents in specialty in vitro and in vivo oncology models. Charles River is the exclusive distributor of JAX™ mice in Europe, including the highly immunodeficient humanized NSG mouse.

www.criver.com

Contact: David Gregory, Research Models and Services Specialist  
Email: cruksd@crl.com  
Phone: +44 (0)1843 823 388  
Fax: +44 (0)1843 823 497  
Manston Road, Margate, Kent, CT9 4LT, UK
**Children with Cancer UK**
Exhibition Stand Unit: 39

Children with Cancer UK (formerly known as Children with Leukaemia) is one of the UK’s leading funders of research into childhood cancer. We fund a broad range of research into childhood cancer — including research into aetiology, treatment and survival — through a variety of mechanisms including project grants and fellowships.

[www.childrenwithcancer.org.uk](http://www.childrenwithcancer.org.uk)

Contact: Katie Martin, Research Manager  
Email: research@childrenwithcancer.org.uk  
Phone: +44 (0)20 7404 0808  Fax: +44 (0)20 7404 3666  
51 Great Ormond Street, London, WC1N 3JQ, UK

**Cronus Technologies / TissueGnostics**  
Exhibition Stand Unit: S1

Cronus Technologies is a leading distributor of advanced technologies from innovative suppliers in cell and molecular oncology. We ensure the best outcomes for research activities using pioneering instruments. High content imaging systems for adherent and suspension cells, cell sorting, genomics and proteomics platforms for high throughput analysis form the core of our portfolio.

[www.cronustechco.co.uk](http://www.cronustechco.co.uk)

Contact: Carole Phelan, Sales Support  
Email: sales@cronustechco.co.uk  
Phone: +44 (0)1276 691 846  Fax: +44 (0)1276 423 493  
4 Camberley Business Centre, Bracebridge, Camberley, Surrey, GU15 3DP
Exhibitor information

**ecancer**
Exhibition Stand Unit: 05

ecancer is the leading oncology channel committed to improving cancer communication and education with the goal of optimising patient care and outcomes. By using the latest technologies, ecancer works closely with leading figures in oncology to inform and educate the global cancer community.

**www.ecancer.org**

Contact: Katie Foxall, Publishing Manager  
Email: katie@ecancer.org  
Phone: +44 (0)117 909 4608  
Fax: +44 (0)117 909 4630  
154 Cheltenham Road, Bristol, BS6 5RL, UK

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**Eurogentec**
Exhibition Stand Unit: 62

Eurogentec, part of Kaneka Corporation, is a supplier of trusted solutions to the Life Science Communities. The Life Science BU proposes reagents for Genomics and Proteomics. The Diagnostic Services BU provides components and services to Molecular Diagnostics. The GMP BioManufacturing BU is a FDA inspected CMO manufacturing cGMP biopharmaceuticals.

**www.eurogentec.com**

Email: info.uk@eurogentec.com  
Phone: +44 (0)1794 511 411  
Fax: +44 (0)1794 522 417  
Old Headmasters House, Unit 1, Building 1, Forest Business Centre, Fawley Road, Fawley, Southampton, SO45 1FJ, UK
European Association for Cancer Research (EACR)
Exhibition Stand Unit: 04

The European Association for Cancer Research (EACR) has one guiding aim ‘The advancement of cancer research’. The Association provides services to members, presents educational, training and scientific meeting opportunities, and facilitates communication and collaboration. With over 10,000 members, the EACR is Europe’s largest member society for cancer research.

www.eacr.org

Contact: Kathryn Wass, Office and Educational Programme Manager
Email: kathryn.wass@nottingham.ac.uk
Phone: +44 (0)115 951 5114 Fax: +44 (0)115 951 5115
Sir Colin Campbell Building, University of Nottingham Innovation Park, Triumph Road, Nottingham, NG7 2TU, UK

European Society for Medical Oncology (ESMO)
Exhibition Stand Unit: 42

ESMO is the leading European professional organisation committed to advancing the specialty of medical oncology and promoting a multidisciplinary approach to cancer treatment. ESMO is committed to good science that leads to better medicine and determines best practice.

ESMO represents a community of over 7,000 oncology professionals from over 120 countries.

www.esmo.org

Email: esmo@esmo.org
Phone: +41 (0)91 973 1900 Fax: +41 (0)91 973 1902
Via Luigi Taddei, 4, 6962 Viganello – Lugano, Switzerland
FluidX Ltd
Exhibition Stand Unit: 66

Our customers store chemical compounds and biological samples for long periods of time to enable them to develop a better understanding of disease processes and help develop new treatments for the future. At FluidX we help this research by providing the storage and tracking products that enable scientists to carry out their research safe in the knowledge that their samples are preserved and identified for decades into the future. Who knows, maybe one day we’ll find that a key treatment is developed with the help of material stored in FluidX 2D-Coded Tubes!

The team at FluidX probably know more about 2D barcoded storage tubes and readers than any other group in the world. We were part of the team that developed the very first 2D datamatrix barcoded tubes back in 1999 and also introduced the first scanner capable of identifying a whole rack of 96 tubes.

www.fluidx.eu

Contact: Emma Ryan, UK Sales Manager
Email: info@fluidx.eu
Phone: +44 (0)1625 861 614 Fax: +44 (0)1625 861 615
Monks Heath Hall Workshops, Chelford Road, Nether Alderley, Cheshire, SK10 4SY, UK

GATC Biotech Ltd
Exhibition Stand Unit: 41

GATC Biotech is Europe’s leading service provider of DNA sequencing with more than 10,000 academic and industrial customers worldwide. For over two decades, we have offered sequencing and bioinformatics solutions from single samples up to large scale projects. GATC Biotech has sequenced more than 5 million samples, ten thousands of bacterial, plant and other whole genomes as well as hundreds of whole human genomes.

www.gatc-biotech.com

Contact: Gemma Hughes
Email: g.hughes@gatc-biotech.com
Phone: +44 (0)20 7691 4921 Fax: +44 (0)20 7691 4923
London BioScience Innovation Centre, 2 Royal College Street, London, NW1 0NH, UK
Genomic Health Inc
Exhibition Stand Unit: 81

Genomic Health, a global health company founded in August 2000 and located in Redwood City, California, is committed to improving the quality of cancer treatment decisions through the research, development and commercialization of genomic-based clinical laboratory services.

www.oncotypedx.com

Contact: Karen Watson, Marketing Communications Specialist
Email: kwatson@genomichealth.com
Phone: +44 (0)20 3440 5153  Fax: +44 (0)20 3440 5151
3 Devonshire Street, London, W1W 5DT, UK

Hospira UK Limited
Exhibition Stand Unit: 6 & 7

Hospira is a global speciality pharmaceutical and medication delivery company dedicated to Advancing Wellness™. As a world expert in speciality generic injectable pharmaceuticals, Hospira offers one of the broadest portfolios of generic acute-care and oncology injectables, as well as integrated infusion therapy and medication management solutions.

www.hospira.com

Contact: Julie Lenihan, Product Manager, Biosimilars & Proprietary Pharmaceuticals
Email: Julie.Lenihan@hospira.com
Phone: +44 (0)1926 835 347
Mobile: +44 (0)7720 084 450
Queensway, Royal Leamington Spa, Warwickshire, CV31 3RW, UK
**Integrated DNA Technologies**

Exhibition Stand Unit: 35

Integrated DNA Technologies (IDT) is a leader in custom biology for the research and diagnostic life science market and serves academic research, biotechnology, and pharmaceutical development. Products include DNA oligos, qPCR assays, and custom gene synthesis to support many applications such as DNA sequencing, SNP detection, and functional genomics.

[www.idtdna.com](http://www.idtdna.com)

Contact: David Hughes, Sales Manager  
Email: custcare@idtdna.com  
Phone: +32 (0)16 28 22 60  
Interleuvenlaan 12A, B-3001 Leuven, Belgium

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**LGC Standards**

Exhibition Stand Unit: 55

LGC Standards provide a range of products and services including reference materials and biological standards. The Life Sciences team within LGC Standards has been ATCC’s distribution partner in Europe for over 10 years, providing comprehensive technical consultancy, training and the delivery of sensitive material. LGC Standards also offers a Cell Line Authentication (CLA) program in collaboration with its Forensics division.

[www.lgcstandards.com/bio](http://www.lgcstandards.com/bio)

Contact: Nick Amiss  
Email: nick.amiss@lgcstandards.com  
Phone: +44 (0)20 8943 7947  
Queens Road, Teddington, Middlesex, TW11 0LY, UK
LI-COR Biosciences UK Ltd
Exhibition Stand Unit: 69


www.licor.com/bio

Contact: Patrick Porps, Team Leader Product Management and Support
Email: bio-eu@licor.com
Phone: +44 (0)1223 422 104 Fax: +44 (0)1223 422 105
St John’s Innovation Centre, Cowley Road, Cambridge, CB4 0WS, UK

Liverpool Cancer Research UK Centre
Exhibition Stand Unit: 12

Scientists and clinicians at Liverpool CR-UK Centre boost key areas of research to produce the greatest benefits for cancer patients. The Centre creates a unique opportunity to work with local communities in raising awareness and highlighting prevention of cancer. In recognition of its achievements, the Centre was awarded Freedom of the City of Liverpool in 2012.

www.lctu.org.uk/home/index.asp and www.liverpoolcancercentre.org.uk/

Contact: Claire Hutchinson, Manager
Email: chutch@liverpool.ac.uk
Phone: +44 (0)151 794 8823 Fax: +44 (0)151 795 5284
Department of Molecular and Clinical Cancer Medicine, University of Liverpool, 200 London Road, Liverpool, L3 9TA, UK
Exhibitor information

Macmillan Cancer Support
Exhibition Stand Unit: 79

Macmillan Cancer Support improves the lives of people affected by cancer. We provide practical, environmental, emotional and financial support. One in three of us will get cancer. We are all affected by cancer. We are a source of support. We are a Force for Change. We are Macmillan.

www.macmillan.org.uk

Contact: Olamide Iyiola
Phone: +44 (0)20 7091 2395   Fax: +44 (0)20 7840 7841
89 Albert Embankment, London, SE1 7UQ, UK

Manchester Cancer Research Centre
Exhibition Stand Unit: 46

The Manchester Cancer Research Centre (MCRC) is a partnership between The University of Manchester, The Christie and Cancer Research UK that brings together world-class research into cancer biology, drug discovery and clinical trials on one site. The MCRC has an integrated approach, which is essential in translating research findings in the laboratory into better treatments for cancer patients.

www.manchester.ac.uk/mcrc

Contact: Esther Walker, Head of Operations
Email: mcrc@manchester.ac.uk
Phone: +44 (0)161 446 3156
The University of Manchester, Wilmslow Road, Manchester, M20 4BX, UK
Marie Curie Cancer Care
Exhibition Stand Unit: 80

Marie Curie Cancer Care is a leading funder of palliative and end of life research to benefit people with terminal illnesses at the end of life.

Visit our stand for information on the Marie Curie Cancer Care Research Programme, our research at our hospices and facilities, and our annual research conference.

www.mariecurie.org.uk/research

Contact: Rhiannon Smith, Research Information Officer
Email: rhiannon.smith@mariecurie.org.uk
Phone: +44 (0)20 091 4154
89 Albert Embankment, London, SE1 7TP, UK

Myeloma UK
Exhibition Stand Unit: 89

Myeloma UK is the only organisation in the UK dealing exclusively with myeloma. We help myeloma patients live longer, with a better quality of life by accelerating the discovery, development of and access to new treatments and help patients and their families cope with everything a diagnosis of myeloma brings.

www.myeloma.org.uk

Contact: Eric Low, Chief Executive
Email: myelomauk@myeloma.org.uk
Phone: +44 (0)131 557 3332 Fax: +44 (0)131 556 9720
Broughton House, 31 Dunedin Street, Edinburgh, EH7 4JG, UK
NCRI is a UK-wide partnership between government, charity and industry, which promotes cooperation in cancer research among its 22 member organisations.

Through our initiatives and the NCRI Cancer Conference, we encourage knowledge sharing and cross-disciplinary collaboration for the benefit of patients, the public and the research community.

www.ncri.org.uk

Contact: Nicola Harris, Communications Manager
Email: info@ncri.org.uk
Phone: +44 (0)20 3469 8460   Fax: +44 (0)20 3014 7658
Angel Building, 407 St John Street, London, EC1V 4AD, UK

Cancer patients and researchers need pathology. At our stand, learn more about what pathologists can do for you. We shall show you the vital importance of cellular pathology in cancer research. We represent the often invisible science of tissue diagnosis, assessing the biological properties of cells that affect how they function.

www.ncri.org.uk

Contact: Bridget Wilkins, NCRI Pathology Lead for NHS Engagement in Biobanking
Email: b.wilkins@nhs.net; bridget.wilkins@gstt.nhs.uk
Phone: +44 (0)20 7188 8542   Mobile: +44 (0)7721 859 138
Cellular Pathology Department, 2nd Floor, N Wing, St Thomas’ Hospital, London, SE1 7EH, UK
NCRI Consumer Liaison Group (NCRN)
Exhibition Stand Unit: 38

A key focus for patient and public involvement (PPI) across the NCRN and NCRI is the Consumer Liaison Group (CLG), a national network of cancer patients and carers working with research teams to help develop and deliver patient focussed research studies. The CLG works through various organisations to ensure information about research provided to patients and the public is easily understood and made widely available.

www.ncrn.org.uk

Contact: Karen Inns, NCRN Patient & Public Involvement (PPI) Lead
Email: ppi@ncrn.org.uk
Phone: +44 (0)113 343 2254   Fax: +44 (0)113 343 2242
NCRN Coordinating Centre, University of Leeds, MacMillan Wing, Fairbairn House, 71-75 Clarendon Road, Leeds, LS2 9PH, UK

New England BioLabs
Exhibition Stand Unit: 34

New England BioLabs supplies molecular biology enzymes and DNA ladders. We also offer a range of PCR reagents, Epigenetic reagents, E. coli expression systems and Competent Cells.

We also supply cancer related activation state specific antibodies such as ROS1 and ALK, ELISA kits and PTMScan services from Cell Signaling Technology.

www.neb.uk.com

Contact: Davin Miller, Sales Manager
Email: info@uk.neb.com
Phone: +44 (0)800 318 486
75-77 Knowl Piece, Hitchin, SG4 0TY, UK
Newcastle Cancer Centre
Exhibition Stand Unit: 90

The Newcastle Cancer Centre is a partnership between Cancer Research UK, Newcastle University, Newcastle Hospitals Foundation Trust, the North of England’s Children’s Cancer Research Fund and the Sir Bobby Robson Foundation to improve cancer treatments for adults and children in the North East and beyond. Public engagement and education are key components of our strategy.

Contact: Ruth Plummer, Professor of Experimental Cancer Medicine, Lead for Newcastle Cancer Centre
Email: ruth.plummer@ncl.ac.uk
Phone: +44 (0)191 213 8476    Fax: +44 (0)191 213 7430
Northern Institute for Cancer Research, Newcastle University, Framlington Place, Newcastle upon Tyne, NE2 4HH, UK

NIHR Cancer Research Network (NCRN)
Exhibition Stand Unit: 36

The NIHR Cancer Research Network (NCRN) provides researchers with the practical support needed to make cancer clinical studies happen in the NHS, so that more research takes place, and more patients can take part.

Our aim is to improve the speed, quality and integration of research, to improve patient care.

www.ncrn.org.uk

Contact: Rachel Moser
Email: enquiries@ncrn.org.uk
Phone: +44 (0)113 343 2254    Fax: +44 (0)113 343 2242
NCRN Coordinating Centre, University of Leeds, MacMillan Wing, Fairbairn House, 71-75 Clarendon Road, Leeds, LS2 9PH, UK
Novartis
Exhibition Stand Unit: 73 & 75

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2012, the Group achieved net sales of USD 56.7 billion, while R&D throughout the Group amounted to approximately USD 9.3 billion (USD 9.1 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 128,000 full-time-equivalent associates and operate in more than 140 countries around the world.

www.novartis.co.uk

Novartis Pharmaceuticals UK Ltd, Frimley Business Park, GB- Frimley/Camberley, Surrey GU16 7SR, UK

Registered in England No. 119006

Olink Bioscience
Exhibition Stand Unit: 64

Olink Bioscience develops, manufactures, and markets unique and highly innovative proprietary products for biomarker research and development. Our groundbreaking tools gain new insights in disease processes, improve disease detection, and contribute to a better understanding of biology which will improve clinical decision making.

www.olink.com

Contact: Mats Bergström, Regional Manager Europe & Asia
Email: info@olink.com
Phone: +46 (0)18 444 3970  Fax: +46 (0)18 50 93 00
Uppsala Science Park, SE-751 83 Uppsala, Sweden
**Onocology News**  
Exhibition Stand Unit: 48

A unique FREE publication for cancer professionals, providing reviews of oncology and related journals in a high quality glossy magazine format. Cancer care professionals value the magazine’s practical and accessible approach and, with a readership of over 6,750 specialists throughout UK, it is the most popular way to keep up-to-date on the latest news.

www.oncologynews.biz

Contact: Patricia McDonnell, Publisher  
Email: Patricia@oncologynews.biz  
Phone: +44 (0)208 289 7023  
Fax: +44 (0)208 289 7023  
88 Camderry Road, Dromore, Co Tyrone, BT78 3AT, UK

**Pancreatic Cancer UK**  
Exhibition Stand Unit: 26

Pancreatic cancer is the 5th most common cause of cancer in the UK, but it has the lowest survival rate of the 21 most common cancers.

We are tackling this by funding innovative research that makes the most impact with limited resources, and leverages additional investment.

Through our Research Innovation Fund we aim to spur creative, cutting edge ideas and approaches in pancreatic cancer research.

www.pancreaticcancer.org.uk

Contact: Amy Wilkinson, Charity Coordinator  
Email: research@pancreaticcancer.org.uk  
Phone: +44 (0)20 7820 6701  
Fax: +44 (0)2088 289 7023  
2nd Floor Camelford House, 89 Albert Embankment, London, SE1 7TW, UK
Pfizer
Non-exhibiting major sponsor

Improving the outlook for cancer patients begins with a focus on strong bonds between Pfizer Oncology and our network of partners. Pfizer Oncology has been working to become a valued partner to the cancer care community and is dedicated to helping improve clinical outcomes, quality patient care and ultimately survivorship.

www.pfizer.co.uk
Contact: Fiona Raisen
Email: fiona.raisen@pfizer.com
Phone: +44 (0)1304 616 161  Fax: +44 (0)1737 332 514
Walton Oaks, Dorking Road, Walton on Thames, Tadworth, Surrey, KT20 7NS, UK

Pierre Fabre Oncology
Exhibition Stand Unit: 27

Pierre Fabre, the second largest independent French pharmaceutical company, has a reputation of top-level scientific, clinical and therapeutic know-how, which has made the Pierre Fabre group one of Europe’s leaders in the cancer field. Pierre Fabre Oncology is currently active in HSCT, breast, bladder and lung cancer.

www.pierre-fabre.com
Email: contactus@pierre-fabre.co.uk
Phone: +44 (0)1962 874 400
Hyde Abbey House, 23 Hyde Street, Winchester, Hampshire, SO23 7DR, UK
Prostate Cancer UK
Exhibition Stand Unit: 77

Prostate Cancer UK fights to help more men survive prostate cancer and enjoy a better quality of life. Our priorities are:

Supporting men and providing information
Finding answers by funding research
Leading change to raise awareness and improve care

We fund research into risk, diagnosis and treatment of prostate cancer.

http://prostatecanceruk.org

Contact: Kate Holmes, Head of Research
Email: research@prostatecanceruk.org
Phone: +44 (0)20 3310 7126
4th Floor, The Counting House, 53 Tooley Street, London, SE1 2QN, UK

QIAGEN
Exhibition Stand Unit: 71

QIAGEN N.V., a Netherlands holding company is the leading global provider of Sample & Assay Technologies that are used to transform biological materials into valuable molecular information.

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www.qiagen.com

Contact: Claire Burrows, Regional Marketing Manager Europe
Email: claire.burrows@qiagen.com
Phone: +44 (0)7966 808 286
Skelton House, Lloyd Street North, Manchester, M15 6SH, UK
Randox Laboratories
Exhibition Stand Unit: 23

With over 30 years’ experience as an international diagnostics company Randox has now focused its innovative and novel tests within Oncology research industries; offering a comprehensive range of accurate arrays and markers to aid future developments.

www.randox.com

Contact: Allen Huxley, UK & Ireland Research Sales Manager
Email: marketing@randox.com
Phone: +44 (0)28 9442 2413
55 Diamond Road, Crumlin, Co. Antrim, BT29 4QY, UK

Roche Products Limited
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For more information: www.roche.co.uk

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Most importantly, we never forget that patients are at the heart of everything we do. They are our inspiration, our motivation and the reason we feel so passionate about our work.

Reference: 1. Roche Historical Archive, F. Hoffmann-La Roche Ltd, Basel 'Traditionally Ahead of our time' 2008: 38

www.roche.co.uk and www.rocheoncology.co.uk

Contact: Keely Parker
Email: keely.parker@roche.com
Phone: +44 (0)1707 367 546 Fax: +44 (0)1707 384 565
Hexagon Place, 6 Falcon Way, Shire Park, Welwyn Garden City, Herts, AL7 1TW, UK

RPS Services Ltd
Exhibition Stand Unit: 54

RPS Services introduce the Faxitron CellRad desk top x-ray cell irradiator. We will also introduce the Faxitron UltraFocus x-ray cabinet imaging system.

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Contact: Robert A Schmid, Managing Director
Email: info@rpsservices.com
Phone: +44 (0)870 979 9900 Fax: +44 (0)870 979 9911
Unit 1A, The Cottage, 100 Royston Road, Byfleet, Surrey, KT14 7NY
Exhibitor information

Science & Technology Facilities Council
Exhibition Stand Unit: 28

We are one of Europe’s largest multi-disciplinary research organisations, and our goal is to deliver World Class Research, Innovation and Skills for the benefit of the United Kingdom and its people — and for the world more broadly.

www.stfc.ac.uk/home.aspx

Contact: Linda Enderby, Futures Stakeholder and Performance Manager
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Phone: +44 (0)1925 603 457
Room B80, Daresbury Laboratory, Sci-Tech Daresbury, Keckwick Lane, Daresbury, Warrington, WA4 4AD, UK

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Exhibition Stand Unit: 85

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Email: mplant@sequenom.com
Phone: +44 (0)161 612 8172  Fax: +44 (0)161 612 8172
Mendelssohnstr 15D, D-22761, Hamburg, Germany
Sigma-Aldrich
Exhibition Stand Unit: 51

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Contact: Debi Chakraborty, Senior Marketing Communication Coordinator
Phone: +44 (0)1202 712 231
Fancy Road, Poole, Dorset, BH12 4QH, UK

Source BioScience Plc
Exhibition Stand Unit: 40

Source BioScience LifeSciences are European leaders in DNA sequencing, genomic services, bioinformatic analyses and offers a comprehensive portfolio of genomic reagents and antibodies. Utilising the Illumina MiSeq and HiSeq2000 platforms, our comprehensive Next generation sequencing service and advanced bioinformatics will accelerate your research.

www.sourcebioscience.com

Email: sales@sourcebioscience.com
Phone: +44 (0)115 973 9012 Fax: +44 (0)115 973 9021
1 Orchard Place, Nottingham Business Park, Nottingham, NG8 6PX, UK
Target Ovarian Cancer
Exhibition Stand Unit: 60

Target Ovarian Cancer is the award-winning national charity working to save lives and help women live their lives to the full, wherever they live in the UK. We do this by

- Funding the national open grants scheme for ovarian cancer
- Improving early diagnosis
- Supporting women

www.targetovariancancer.org.uk

Contact: Simon Newman, Head of Research
Email: snewman@targetovarian.org.uk
Phone: +44 (0)20 7923 5477  Fax: +44 (0)20 7923 5471
30 Angel Gate, City Road, London, EC1V 2PT, UK

The Brain Tumour Charity
Exhibition Stand Unit: 37

The Brain Tumour Charity is committed to fighting brain tumours on all fronts. We fund scientific and clinical research into brain tumours and offer support and information to those affected, whilst also raising awareness. The HeadStart: be brain tumour aware campaign aims to reduce diagnosis times of childhood brain tumours, through raising awareness of the signs and symptoms.

www.thebraintumourcharity.org

Contact: Alison Evans, Head of Research and Policy
Email: alison.evans@thebraintumourcharity.org
Phone: +44 (0)1252 749 440
Hartshead House, 61-65 Victoria Road, Farnborough, GU14 7PA, UK
The College of Radiographers
Exhibition Stand Unit: 24

The College of Radiographers is committed to developing the science and practice of radiography, radiotherapy, and clinical imaging, including ultrasound, nuclear medicine and magnetic resonance imaging. We promote study and research and make major contributions to health policy development in these fields.

www.sor.org

Contact: Charlotte Beardmore, Professional and Education Manager
Email: info@sor.org
Phone: +44 (0)20 7740 7200 Fax: +44 (0)20 7740 7233
207 Providence Square, Mill Street, London, SE1 2EW, UK

The Francis Crick Institute
Exhibition Stand Unit: 50

The Francis Crick Institute will be an interdisciplinary medical research institute. Its work will help understand why disease develops and find new ways to prevent and treat illnesses such as cancer, heart disease and stroke, infections, and neurodegenerative diseases. Due to open in 2015, it will employ 1,500 staff, including 1,250 scientists.

www.crick.ac.uk

Contact: Alexandra Hartnall, Communications Manager
Email: info@crick.ac.uk
Phone: +44 (0)800 028 6731
215 Euston Road, London, NW1 2BE, UK
The Institute of Cancer Research
Exhibition Stand Unit: M4

The Institute of Cancer Research, London is one of the world’s most influential cancer research institutes. We lead the world in isolating cancer-related genes and discovering new targeted drugs for personalised cancer treatment. The Institute of Cancer Research (ICR) is a college of the University of London and ranked as the top academic research institute in the UK. We have charitable status and rely on support from partner organisations, charities and donors.

Meet Deputy CEO Professor Paul Workman at our stand on Monday 4 November at 12.50.

www.icr.ac.uk

Contact: Lauren King, Communications Assistant
Email: lauren.king@icr.ac.uk
Phone: +44 (0)20 7153 5136
123 Old Brompton Road, London, SW7 3RP, UK

The Royal College of Radiologists
Exhibition Stand Unit: 86

The Royal College of Radiologists (RCR) leads, supports and educates in medical imaging and cancer treatment. The RCR sets the stand for practice in and the specialties of clinical oncology and clinical radiology and shapes their future for the benefit of patient care.

www.rcr.ac.uk

Email: enquiries@rcr.ac.uk
Phone: +44 (0)20 7405 1282
63 Lincoln’s Inn Fields, London, WC2A 3JW, UK
University College London Cancer Institute
Exhibition Stand Unit: M1

The vision of UCL with our partner healthcare system is to become an international hub of excellence in cancer research, training and clinical care. With over 130 Groups researching cancer and with a total research grant income of over £160 million, UCL is developing into a major cancer force.

www.ucl.ac.uk/cancer

Contact: Kay Tott, Deputy Institute Manager
Email: k.tott@ucl.ac.uk
Phone: +44 (0)20 7679 6700  Fax: +44 (0)20 7679 6817
The Paul O’Gorman Building, 72 Huntley Street, London, WC1E 6BT, UK

VisualSonics
Exhibition Stand Unit: 08

VisualSonics is the undisputed world leader in real-time, in vivo, microimaging systems, providing modalities specifically designed for preclinical cancer research. Our systems deliver outstanding image quality and resolution and provide tools for fast, accurate 3D tumour sizing, biomarker analysis, and sophisticated angiogenesis / tumour perfusion quantification.

www.visualsonics.com

Contact: Angela Kost, European Sales and Administrative Assistant
Email: akost@visualsonics.com
Phone: +31 20 751 2020
Science Park 402, 1098 XH Amsterdam, The Netherlands
Wales Cancer Research Network
Exhibition Stand Unit: 67

Wales Cancer Research Network is part of the National Institute for Social Care and Health Research Clinical Research Centre (NISCHR CRC). NISCHR CRC provides an expert all-Wales workforce to support research activity, delivers a high quality training programme, co-ordinates public involvement in research and manages the NISCHR clinical research portfolio.

www.wcrn.wales.nhs.uk

Contact: Jayne Caparros, Research Network Manager, NISCHR CRC Lead for Cancer
Email: wcrn@wales.nhs.uk
Phone: +44 (0)2920 196 808 Fax: +44 (0)2920 196 817
3rd Floor, 12 Cathedral Road, Cardiff, CF11 9LJ, UK

Warwick Clinical Trials Unit
Exhibition Stand Unit: 61

Warwick Clinical Trials Unit (WCTU) is an academic unit undertaking clinical trials addressing issues of local, national and international importance.

All cancer trials are NIHR adopted and seek to change clinical practice.

www2.warwick.ac.uk/fac/med/research/hscience/ctu/

Contact: Helen Higgins, Senior Project Manager
Email: h.higgins@warwick.ac.uk
Phone: +44 (0)2476 151 178 Fax: +44 (0)2476 151586
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Exhibition Stand Unit: 88

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3. Oncology Journal Watch
   A round-up of relevant published research in different clinical areas, written by Dr Adam Dangoor, Consultant Medical Oncologist at Bristol Haematology and Oncology Centre.
   www.doctors.net.uk/oncologyJW

4. NCIN Cancer Outcomes Conference 2013
   Dr Georgios Lyratzopoulos shares his highlights from the conference including a talk on the current “revolution” in cancer intelligence due to the explosion of new data.
   www.doctors.net.uk/NCIN2013

5. Overview from ASCO Annual Meeting
   Read articles and listen to interviews with presenters about some of the key data presented at this year’s conference. Funded by Roche.
   www.doctors.net.uk/ASCO2013

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For more information visit conference.ncri.org.uk
The NCRI Cancer Conference is a team effort involving many staff from the NCRI Secretariat, Cancer Research UK, other NCRI partners and contractors.

**NCRI Cancer Conference Secretariat**

The Conference Secretariat, under the leadership of outgoing Director Jane Cope, have been instrumental in organising this event. The team will be onsite for the whole Conference. Please feel free to speak to them for any feedback or ideas. Ask at the General Enquiries desk to find them onsite; alternatively, send an email and they will get back to you: ncriconference@ncri.org.uk.

Lorretta Amajoutt, Senior Administrator  
Laure-Anne Garnier, Development Manager  
Kirsty Lyons, Programme Officer  
Sharon Vanloo, Operations Manager  
Deborah Williams, Administrator (Programme, Communications and Marketing)

**H2 Events**

Thank you to Sue Harrison, Sam Harrison and all the team at H2 Events for the design and production of the exhibition stands.

**Press and media**

Thanks to Laura Dibb, Steve Palmer and other colleagues from the Cancer Research UK press office.

**Design and web**

Thank you to Callisto Design, Tracey Goodland, RF design, Peter Mahoney and Jack Towner for the design of the Conference materials and website.

**Other NCRI Secretariat staff**

Thank you to all NCRI staff members for their input and support. Please enquire at the NCRI stand in Hall 2 if you wish to speak with anyone on this list.

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Rachael Brannan, Research Officer, National Cancer Intelligence Network (NCIN)  
Anne Carter, Portfolio Lead  
Laura Chambers, Personal Assistant/Senior Administrator (Clinical Studies Groups)  
Carolyn Chan, Programme Manager (Radiotherapy)  
Michelle Cox, Research Project Officer (Clinical Studies Groups)  
Nanita Dalal, Administrator (Clinical Studies Groups)  
Rachel Doxford, Administrator  
Alexandra Ferguson, Programme Manager (Surgery and Imaging)  
Lorna Fern, Research Development Co-ordinator (Clinical Studies Groups)
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Karen Kennedy, Incoming Director
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Jack Towner, Creative and Technical Officer
Ulla Ventham, Administrator/Secretary (Clinical Studies Groups)
Thomas White, Research Analyst

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## Acronyms

This is an evolving list, and we know that things move quickly so if you spot any inaccuracies or have some other terms to add, please email us at info@ncri.org.uk.

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<tr>
<th>A</th>
<th>ABPI</th>
<th>Association of the British Pharmaceutical Industry (an umbrella organisation to which many of the pharmaceutical companies in the UK belong)</th>
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<tr>
<td>ACoRD</td>
<td>Attributing the Costs of health and social care Research and Development (a framework for the NHS and its partners which clarifies the distinction between research costs, NHS support costs and treatment costs)</td>
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<td>AHSN</td>
<td>Academic Health Science Network (local partnership working in England, new in 2012, which brings together academia, industry and the NHS to identify and deliver innovations into healthcare)</td>
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<tr>
<td>AICR</td>
<td>Association for International Cancer Research (a research funder and member of the NCRI Partnership)</td>
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<tr>
<td>AMRC</td>
<td>Association of Medical Research Charities (a membership organisation of the leading medical and health research charities in the UK)</td>
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<tr>
<td>AMS</td>
<td>The Academy of Medical Sciences (an independent body that promotes advances in medical science and campaigns to ensure these are translated into healthcare benefits for society)</td>
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<tr>
<td>APPGC</td>
<td>All Party Parliamentary Group on Cancer (brings together MPs and Peers to help improve cancer services)</td>
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<tr>
<td>ARSAC</td>
<td>Administration of Radioactive Substances Advisory Committee (provides governance over radioactive medicinal products in the UK)</td>
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<tr>
<td>B</td>
<td>BBSRC</td>
<td>Biotechnology and Biological Sciences Research Council (UK public funder of non-medical bioscience for scientific research institutes and university research departments in the UK, and member of NCRI Partnership)</td>
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<table>
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<tr>
<th>C</th>
<th>CaRD</th>
<th>Cancer Research Database (an NCRI database of the cancer research funded by all its partners, with data collected each year and available online)</th>
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<tr>
<td>CCB</td>
<td>Confederation of Cancer Biobanks (an NCRI initiative that brings together different biobanks that hold tissue samples in the UK to work more closely)</td>
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<tr>
<td>CCLG</td>
<td>Children’s Cancer and Leukaemia Group (a charity for children and young people with cancer and leukaemia)</td>
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<tr>
<td>CCG</td>
<td>Clinical Commissioning Group (set up by the Health and Social Care Act 2012 to organise the delivery of NHS services in England)</td>
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<tr>
<td>CCRN</td>
<td>Comprehensive Clinical Research Network (part of the NIHR Clinical Research Network which provides support for clinical trials and well designed studies in all areas of disease and clinical need)</td>
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<tr>
<td>CLG</td>
<td>Consumer Liaison Group (a group made up of ‘consumers’ with current or recent experiences of cancer services as patients, carers, relatives, or members of the public, which aims to improve the quality and value of cancer research and help to raise public awareness)</td>
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<tr>
<td>CLRN</td>
<td>Comprehensive Local Research Network (25 local areas across England that collectively form the CCRN)</td>
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<tr>
<td>CPRD</td>
<td>Clinical Practice Research Datalink (a service designed to maximise the way anonymised NHS clinical data can be linked)</td>
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<tr>
<td>CR-UK</td>
<td>Cancer Research UK (a cancer charity and member of the NCRI Partnership)</td>
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<tr>
<td>CSG</td>
<td>Clinical Studies Group (an NCRI group that brings together appointed researchers to develop a strategic portfolio of studies)</td>
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<td>Acronyms</td>
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<tr>
<td>CSO</td>
<td>Chief Scientist Office (part of the Scottish Government which supports research in Scotland and advises the Scottish Government on how research contributes to improvements in health and healthcare. Also a member of the NCRI Partnership)</td>
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<tr>
<td>CSP</td>
<td>Coordinated System for gaining NHS Permission (an NIHR system to standardise and simplify the process of gaining NHS Permission for commercial and non-commercial clinical research studies in England)</td>
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<tr>
<td>CTIMP</td>
<td>Clinical Trial of an Investigational Medical Product (a study that looks at the safety or efficacy of a medicine/foodstuff/placebo in humans, as defined by the Medicines for Human Use (Clinical Trials) Regulations 2004)</td>
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<tr>
<td>CTAAC</td>
<td>Clinical Trials Awards and Advisory Committee (a CR-UK funding stream, mostly for phase II and III trials)</td>
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<td>CTRad</td>
<td>Clinical and Translational Radiotherapy Research Working Group (an NCRI initiative that supports radiotherapy research)</td>
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<tr>
<td>CTU</td>
<td>Clinical trials unit (specialised biomedical research unit which designs, centrally coordinates and analyses clinical trials and other studies)</td>
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<tr>
<td>eolcRIG</td>
<td>End of Life Care Research Interest Group (an NCRI initiative which brings together health research funders, care providers and related charities who promote high quality research in end of life care)</td>
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<tr>
<td>EORTC</td>
<td>European Organisation for the Research and Treatment of Cancer (an organisation that delivers trials, workshops and other Europe-wide initiatives in cancer)</td>
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<tr>
<td>EPSRC</td>
<td>Engineering and Physical Sciences Research Council (a research funder)</td>
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<tr>
<td>ESRC</td>
<td>Economic and Social Research Council (a research funder and member of the NCRI Partnership)</td>
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<tr>
<td>FP7</td>
<td>Seventh Framework Programme for research and technology development (a channel for researches in the European Community to access funding for trans-national collaborative research, or personal awards)</td>
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<tr>
<td>FTE</td>
<td>Full-time equivalent (a commonly used unit of measuring the amount of time that members of staff are employed or have time allocated to particular projects)</td>
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<tr>
<td>GCLP</td>
<td>Good Clinical Laboratory Practice (a system of management controls for research laboratories and organisations to ensure the uniformity, consistency, reliability, reproducibility, quality, and integrity of non-clinical tests)</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice (a set of guidelines that must be followed when conducting clinical trials to ensure that the rights and well-being of trial participants are protected and that data generated in the trial is valid)</td>
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<tr>
<td>GPRD</td>
<td>General Practice Research Database (UK database containing anonymised medical records from primary care)</td>
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<td>GRIST</td>
<td>Growing Recruitment to Interventional Surgical Trials (the name of a surgical working group, funded by the NIHR)</td>
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<td>HES</td>
<td>Hospital episode statistics (an NHS database that records details of hospital admissions, outpatient appointments and A&amp;E appointments at NHS hospitals in England)</td>
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<td>HRA</td>
<td>Health Research Authority (an NHS Special Health Authority to protect and promote the interests of patients and the public in health research)</td>
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<tr>
<td>HSC</td>
<td>Health and Social Care (the Northern Irish government department responsible for health research, and a member of the NCRI Partnership)</td>
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<tr>
<td>HTA (1)</td>
<td>Health Technology Assessment (an NIHR funding stream for research to evaluate healthcare treatments or tests)</td>
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<tr>
<td>HTA (2)</td>
<td>Human Tissue Authority (ensures that human tissue is used safely and ethically, and with proper consent)</td>
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<td>ICRP</td>
<td>International Cancer Research Partnership (an alliance of cancer organisations, including NCRI, that works to enhance global collaboration and strategic coordination of research)</td>
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<tr>
<td>IMI</td>
<td>Innovative Medicines Initiative (European public-private initiative aiming to speed up the development of better and safer medicines for patients)</td>
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<tr>
<td>IMP</td>
<td>Investigational Medicinal Product (a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial)</td>
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<td>INVOLVE</td>
<td>(part of the NIHR, a national advisory group that supports greater public involvement in NHS, public health and social care research)</td>
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<td>IRAS</td>
<td>Integrated Research Application System (a UK-wide system that streamlines the process for applying for permissions and approvals to conduct health and social care research)</td>
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<td>IRCI</td>
<td>International Rare Cancers Initiative (a strategic collaboration between Cancer Research UK, the UK National Institute for Health Research Cancer Research Network, the US National Cancer Institute, and the European Organisation for Research and Treatment of Cancer to support the development of international clinical trials for rarer cancers)</td>
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<tr>
<td>LICR</td>
<td>Ludwig Institute for Cancer Research (a research funder and member of the NCRI Partnership)</td>
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<tr>
<td>LLR</td>
<td>Leukaemia &amp; Lymphoma Research (a cancer charity and member of the NCRI Partnership)</td>
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<tr>
<td>MHRA</td>
<td>Medicines and Healthcare products Regulatory Agency (an organisation that regulates medicines and medical devices in the UK to ensure they work and are safe)</td>
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<tr>
<td>MRC</td>
<td>Medical Research Council (a research funder and member of the NCRI Partnership)</td>
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<tr>
<td>NAEDI</td>
<td>National Awareness and Early Diagnosis Initiative (England-based initiative that includes activities and research to promote the earlier diagnosis of cancer)</td>
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<tr>
<td>NCEI</td>
<td>National Cancer Equality Initiative (a Department of Health initiative to prompt more research on inequalities and to provide policy advice)</td>
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<tr>
<td>NCI</td>
<td>National Cancer Institute (coordinates the US National Cancer Program and conducts and supports a range of activities related to the causes, prevention, diagnosis, and treatment of cancer)</td>
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<td>Acronym</td>
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<tr>
<td>NCIC</td>
<td>National Cancer Institute of Canada (now the Canadian Cancer Society Research Institute which supports researchers through the administration of cancer research funding)</td>
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<tr>
<td>NCIN</td>
<td>National Cancer Intelligence Network (UK-wide for initiative improving and using the information collected about cancer patients for analysis, publication and research)</td>
</tr>
<tr>
<td>NCRI</td>
<td>National Cancer Research Institute (a partnership of UK research funders that supports coordination in cancer research)</td>
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<tr>
<td>NCRN</td>
<td>National Institute for Health Research Cancer Research Network (a managed research network that supports cancer trial delivery, through the provision of research nurses, data managers and other network staff)</td>
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<tr>
<td>NCSI</td>
<td>National Cancer Survivorship Initiative (works to improve the ongoing services and support available for those living with and beyond cancer)</td>
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<tr>
<td>NICTN</td>
<td>Northern Ireland Cancer Trials Network (umbrella organisation responsible for the coordination of cancer clinical trial activity throughout Northern Ireland)</td>
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<tr>
<td>NIHR</td>
<td>National Institute for Health Research (part of the Department of Health; commissions and funds NHS, social care and public health research in England)</td>
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<tr>
<td>NIHR CRN</td>
<td>National Institute for Health Research Clinical Research Network (the umbrella under which other English research networks, including NCRN, fall)</td>
</tr>
<tr>
<td>NISCHR</td>
<td>National Institute for Social Care and Health Research (Welsh Government department that develops strategy and policy for research in the NHS and social care, and a member of the NCRI Partnership)</td>
</tr>
<tr>
<td>NOCRI</td>
<td>NIHR Office for Clinical Research Infrastructure (aims to simplify the clinical research environment in the UK, and help research funders to navigate NHS infrastructure)</td>
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<tr>
<td>NPRI</td>
<td>National Prevention Research Initiative (a national collaborative initiative that provides funding to support research into chronic disease prevention)</td>
</tr>
<tr>
<td>O</td>
<td>Office for Strategic Coordination of Health Research (takes an overview of the budgetary division and research strategy of both the MRC and NIHR, to ensure both of these government funding streams work in synergy)</td>
</tr>
<tr>
<td>PC-Uk</td>
<td>Prostate Cancer UK (a cancer charity and member of the NCRI Partnership)</td>
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<tr>
<td>PET</td>
<td>Positron emission tomography (a type of medical imaging that can be used in cancer)</td>
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<tr>
<td>PHE</td>
<td>Public Health England (executive agency of the Department of Health, with responsibility for public health)</td>
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<tr>
<td>PPI</td>
<td>Patient and public involvement (a commonly used term for referring to the involvement of lay representatives in a variety of healthcare activities)</td>
</tr>
<tr>
<td>QA</td>
<td>Quality Assurance (processes, activities or programs to assure or improve the quality of research in a defined setting)</td>
</tr>
<tr>
<td>RCR</td>
<td>Royal College of Radiologists (Royal College for the specialities of clinical oncology and radiology)</td>
</tr>
<tr>
<td>RCUK</td>
<td>Research Councils UK (strategic partnership of the UK’s Research Councils)</td>
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<tr>
<td>RfPB</td>
<td>Research for Patient Benefit (an NIHR funding stream for regionally-derived applied research projects in health services and social care)</td>
</tr>
<tr>
<td>RTTQA</td>
<td>Radiotherapy trials quality assurance (a group working to unify, simplify and streamline the QA process for radiotherapy in research)</td>
</tr>
</tbody>
</table>
### Acronyms

<table>
<thead>
<tr>
<th>S</th>
<th>SCRN</th>
<th>Scottish Cancer Research Network (an umbrella organisation to increase, support and sustain clinical trial activity in cancer care, in partnership with the UKCRC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSCRG</td>
<td>Site-specific clinical reference group (established by NCIN to ensure that the data now available is used to improve clinical care and to advise on what data needs to be collected and what analyses conducted)</td>
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<tr>
<td>STFC</td>
<td>Science and Technology Facilities Council (one of the UK’s publicly funded Research Councils responsible for supporting, coordinating and promoting research, innovation and skills development)</td>
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<tr>
<td>STRATUM</td>
<td>Strategic Tissue Repository Alliance Through Unified Methods (a collaborative biobanking project between the pharmaceutical industry and academia)</td>
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<tr>
<td>SuPaC</td>
<td>Supportive and Palliative Care Collaborative (an NCRI initiative to encourage more collaboration and interdisciplinary working in supportive and palliative care)</td>
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<tr>
<td>T</td>
<td>TSB</td>
<td>Technology Strategy Board (a UK public body operating at arm’s length from the Government which offers support and funding to help develop new products and services)</td>
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<tr>
<td>TYA</td>
<td>Teenage and Young Adult (a commonly used acronym when talking about trials involving this age group)</td>
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<tr>
<td>U</td>
<td>UKCRC</td>
<td>United Kingdom Clinical Research Collaboration (a partnership of major stakeholders that influence clinical research in the UK, working collaboratively to address common goals)</td>
</tr>
<tr>
<td>W</td>
<td>WCTN</td>
<td>Wales Cancer Trials Network (an umbrella organisation for cancer clinical researchers in Wales which aims to improve the infrastructure for cancer clinical research)</td>
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<tr>
<td>X</td>
<td>Y</td>
<td>Yorkshire Cancer Research (a cancer charity and member of the NCRI Partnership)</td>
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</table>
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