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IN THIS ISSUE

ON THE COVER

Wendy Fulcher with a portrait of her and her late husband John – turn to page 153

Denys Wheatley
Editor

Cancer – a problem of too much information on the internet?

A year ago I mentioned that we might worry that people are receiving too much information about cancer via social media and campaigning [1]. For those who find it difficult, sometimes repulsive, to consider they have some pathological condition (especially cancer), this deluge of information can be stressful, probably turn some away from learning about the warning symptoms.

For those who take an interest, what should they believe? If new findings have been sufficiently argued from good research or strong circumstantial evidence presented by experts, come from reliable and respected sources, and that are not presented in unguarded terms, but take into account important compounding factors, it seems worthwhile going public. However, the interface between what the experts say and what a PR department or freelance journalist does with the information is another matter. Most information comes from organisations, charities, cancer groups and individuals, not from perusal of learned journals. Slackness in reporting, e.g. for the sake of a "good news story", should be discouraged; but how? The more information on the media, the more tittle-tattle will appear, which will be unhelpful to the general public. Remember that unstressed happy people live longer with stronger defences (especially immunological) than stressed people.

A quick look at the web reveals a plethora of "posts" on cancer. Some are superficial, trivial and sometimes wrong; many give an unbalanced view, lacking consideration of compounding factors. The problem is to separate the "wheat from the chaff", but the man in the street is not an expert and will find this difficult.

What is the internet currently telling us about cancer and its problems [2]. Just as there is concern over a leaked government document, we need to check the major sources of information on cancer, how authentic and reliable they are, but this requires more insight by the reader (see below). One recent report on both television and internet refers to mole counting on the right arm (is the left arm not as good?) giving as reliable a guide to the risk of melanoma as counting them over the whole body. This may worry people, especially those exposing themselves in sunny climes. Another report relates that lemon juice might prevent breast cancer cells becoming invasive. A third considers eating red meat (particularly processed meat, e.g. hamburgers) increases the risk of colon cancer (an issue debated for decades). However, if you drink a lot of green tea your chances of developing colon cancer are lower (so what if you eat a lot of processed red meat and drink plenty green tea?!). Fertility drugs might raise the risk of cancer; some thyroid drugs may increase lung cancer; the entries go on and on. Since these reports emanate from many sources, most lacking contextual relevance, we must ask whether publicity on this scale does the general public a service.

While a lot might come under my heading of "tittle-tattle", unfortunately some cases contain elements of truth that should make us more aware of certain dangers and therefore be prepared to look deeper into the issue. As we are living longer, the danger increases; Cancer Research UK now tells us [3] that 1 in 2 of us will develop cancer in his or her lifetime, a frightening thought to many folk.

Overload of information means that people might take less rather than more notice of cancer issues, which is why we need to educate the general public not only about the prevention and early diagnosis of cancer through reliable information, but educate them into how to judge this reliability in the first place – not an easy task. Failure to do so could have two outcomes; first, without this "training", the dread of developing cancer becomes exacerbated, making matters worse. Second, the situation might be likened to that now confronting the use of social media, i.e. overloading starts to turn people against it. Ignoring reliable information on cancer will certainly not help early diagnosis; it is better to have some reliable information than none.

"There is so much we still need to learn about cancer, and research does not seem to slacken pace. As new findings emerge, people are being bombarding people with too much information, which might or might not be a bad thing. However, this is a problem that now needs to be addressed"

REFERENCES

1. Wheatley DN. *Cancer – Campaigns, Awareness and Education.* Oncology News. 2014;9(5):151.
2. I am not referring to individual post; browse the web with search words such as Cancer Problems and you will see more than enough.
3. www.cancerresearchuk.org – 1 in 2 people will develop cancer.

HELP PREVENT SREs* IN ADULT PATIENTS WITH BONE METASTASES FROM SOLID TUMOURS[1]

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*SREs: skeletal-related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours

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References: 1. XGEVA® (denosumab). Summary of Product Characteristics. 2. Coleman R et al. Ann Oncol 2014;00:1-14.doi: 10.1093/annonc/mdu103.

PRESCRIBING INFORMATION CAN BE FOUND OVERLEAF

Meet the Editorial Team

Professor Denys Wheatley is Editor, and is Director of BioMedES. He has strong research ties in Albany, Davis, Auckland, Valencia, Detroit, Budapest, St Petersburg, Heidelberg, Zürich and Hong Kong. He is eager to establish strong interaction with cancer and cell biology teams worldwide, and initiate programmes in the areas in which his expertise lies. His work in cancer research, other scientific fields, with IFCB, and in publishing and scientific communication has led to his receiving awards in recent years.

Dr Richard J Ablin (Associate Editor), is Professor, Pathology, University of Arizona College of Medicine and a Member of the Arizona Cancer Center, Tucson, Arizona. He received the First Award for scientific excellence from The Haakon Ragde Foundation for Advanced Cancer Studies. Dr Ablin discovered prostate-specific antigen (PSA) in 1970. A pioneer of cryosurgery and cryoimmunotherapy, he has extensive experience in cancer research.

Alan Cooper is Assistant Co-Editor – Urology, and is Lead Scientist with the urology research group in Southampton University Hospitals and senior lecturer (albeit with virtually no lecturing burden) in the Department of Biomedical Sciences at Portsmouth University.

Mr Richard Novell is Assistant Co-Editor – Gastrointestinal Section, and is a Consultant Colorectal Surgeon at the Royal Free Hospital. He was a member of the Court of Examiners of the Royal College of Surgeons for eight years and has been an advisor to NICE, NCEPOD and CORESS, the Confidential Reporting System in Surgery.

Dr Miriam Dwek is Assistant Co-Editor – Breast Cancer, she is a Senior Lecturer in Biochemistry at the Department of Molecular and Applied Biosciences, School of Life Sciences, University of Westminster in London.

Prof Mohammed RS Keshtgar BSc, FRCSI, FRCS (Gen), PhD is Assistant Co-Editor – Breast Cancer, and is a Professor of Cancer Surgery and Surgical Oncology, Royal Free London Foundation Trust. His main area of interest is minimally invasive approaches in diagnosis and treatment of breast cancer. His research interest is in sentinel node biopsy, intra-operative radiotherapy, quantum dot nanotechnology in breast cancer.

Professor Geoffrey J Pilkington is Assistant Editor Neuro-Oncology, is a Professor of Cellular and Molecular Neuro-oncology at the Institute of Biomedical and Biomolecular Sciences, Portsmouth. His research focuses on the development of models for the study of intrinsic brain tumours, elucidation of their metabolism and mechanisms underlying diffuse local invasive behaviour.

Farrokh Pakzad is Assistant Editor – Skin Cancer, and is currently Consultant Oncoplastic Breast and Melanoma Surgeon at Royal Surrey County Hospital. His main areas of specialist interest are in the management of breast disease, oncoplastic and reconstructive breast surgery and the management of skin cancers, in particular, melanoma. Farrokh completed his higher surgical training in London, during which he was selected onto the highly competitive National Oncoplastic Fellowship program.

Dr Constantino Carlos Reyes-Aldasoro is Assistant Editor – Image Analysis. He is a Lecturer in Biomedical Image Analysis at the School of Engineering and Mathematical Sciences, City University London. He has developed a unique portfolio of interdisciplinary skills that span from the acquisition of microscopical images to the analysis of biomedical datasets such as magnetic resonance, computed tomography and microscopy to advanced computer programming and website development.

Mriganka De is Assistant Editor – Head & Neck Oncology. Mr De is a Consultant ENT/Head and Neck surgeon at Royal Derby Hospital, Derby. His interest is head and neck cancer with particular focus on management of early laryngeal cancers.

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Contents

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MR-guided-HIFU for pain palliation of bone metastases

A new clinical multi-centre trial is underway to assess the effectiveness of pain palliation in bone metastases using the Philips Sonalleve MR-HIFU (High Intensity Focused Ultrasound.) Researchers at The Royal Marsden and The Institute of Cancer Research, London are currently participating in this trial and this article outlines the clinical context and our experience on the study so far.

What is HIFU?

In the same way that sunlight can be focused using a lens, ultrasound can be focused using a concave transducer. When performed at high intensity, this focused ultrasound can be used therapeutically. Whereas diagnostic applications use ultrasound intensities ranging from 0.01-0.1 W/cm^2, HIFU uses a range of 800-1500 W/cm^2 to produce an effective ablation.

At the focus, the heating of the tissues is achieved through conversion of the mechanical energy of the sound wave into heat energy as it passes through tissue. To produce ablation, the temperature must be raised to around 60°C for >1 second. As the ultrasound beam has a low energy outside of the focus, it passes through other tissues it moves through without heating or damage.

MR-guided HIFU

Ultrasound-guided HIFU allows real time visualisation of a target volume during therapy and has mostly been used for ablations in the prostate and some abdominal tumours. More recently, MR-guided (MRg) HIFU has become available and this has many obvious advantages. It provides higher resolution images for more accurate planning and targeting, real time temperature monitoring and immediate post-treatment imaging to assess ablations.

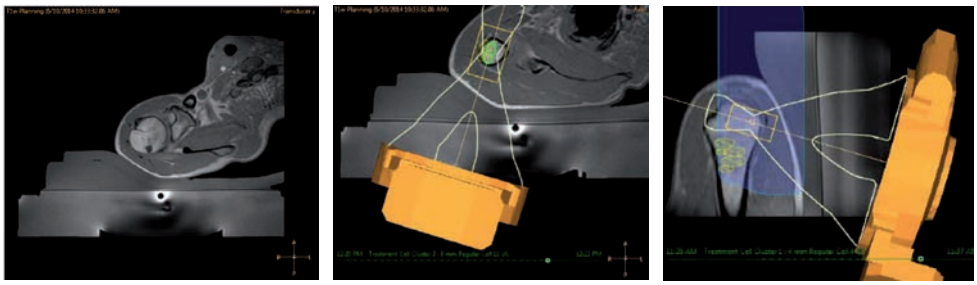
Around 25,000 patients with uterine fibroids have been treated with MRg HIFU so far across the world. At The Royal Marsden and The Institute of Cancer Research (ICR) we are working with its second major application: pain palliation of bone metastases.

The need for MRg-HIFU in bone metastases

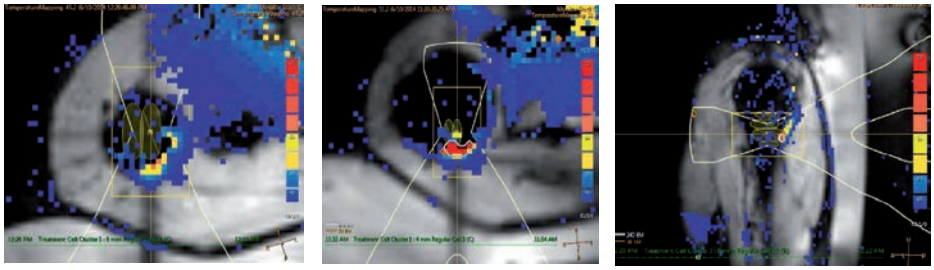
Some patients have residual pain after palliative radiotherapy and can't be safely or effectively re-irradiated. Bone metastases can be extremely painful for several reasons:

- Bone destruction
- Increased sensory innervation (more nerve cell fibres)

Targeting the lesion:



Temperature mapping during sonication:



PRFS images acquired during sonication; red pixels indicate heating >57°C, indicative of achieving heating capable of ablating periosteal nerves.

Patients need to be positioned so that the target area of disease is directly above the HIFU transducer and that is checked using high resolution MR imaging. Once satisfied with the position, the HIFU treatment is planned as a series of separate exposures, called sonications, using these graphical overlays included in the planning software.'

Image credited to the Royal Marsden and the ICR.

- Sensitisation of those nerve cell fibres (nociceptors)
- Distension of the periosteum (fibrous membrane covering the bones) 20.01.15 MRv3

The way that HIFU is thought to alleviate pain is by heating and ablating the nerves of the periosteum (thermal denervation) but there may also be an effect of tumour necrosis giving a reduced mass effect, thus relieving periosteal distension.

Our clinical trial

There have been a number of studies since 2007 which have shown evidence that MRg HIFU can be a safe and effective treatment option for palliation of pain from bone metastases. New purposely-designed equipment has now become available in the form of the Philips Sonalleve MRg HIFU. Using this system, we are involved in a trial which will evaluate HIFU as a treatment option in adult patients with painful bone metastases that have not responded to "standard of care" treatments, including radiotherapy.

The eligibility criteria are very tight and the patient's most painful lesion can be up to 8cm in its largest dimension and must be at least 1cm below the skin.

The primary endpoint of the study is pain response 30 days post treatment. A successful outcome is achieved if there is a reduction in pain scores or reduction in analgesic use. Secondary endpoints include: quality of life assessment; pain response at 60 and 90 days; and changes in lesion size.

Philips Sonalleve system

Our Philips Sonelleve system was installed when the ICR and The Royal Marsden were jointly made a Focused Ultrasound Centre of Excellence. It uses our Philips 3T Achieva MR system in a standard dual-purpose scanning room. The Sonalleve table slides over the lowered MR table so we do not have to remove it.

The Sonalleve's ultrasound transducer sits in an oil bath beneath a window that's covered in a thin membrane. It can focus to a point 14cm above its centre and can be moved and angled to target a lesion as accurately as possible. It has 256 independent channels, an ultrasound frequency of either 1.2 or 1.45 MHz and a maximum acoustic power of 300 watts. The single surface coil for imaging is used in conjunction with another coil that sits underneath the membrane.

Treatment planning

MR images are first acquired on the Achieva and then imported into the Sonalleve. A graphical representation of the proposed ultrasound beam allows us to visualise which tissues we're going to pass through as we target the lesion.

A number of treatment cells can cover one lesion varying in size from 2-16mm in diameter. Their shape is determined by the way the transducer steers the beam in concentric circles, starting at the centre, to build up each treatment cell. The ultrasound's intensity for each treatment cell can also be varied.

Preparing the patient

Prior to treatment, patients attend screening visits to establish their eligibility for the study, which includes physical examination, pain assessment and MRI scanning. On the treatment day, patients are admitted as day cases and seen by an anaesthetist. We know that patients experience pain as the treatment is delivered, so we need to manage this whilst making sure they stay still. After establishing IV access, the 20.01.15 MRv3 patient is helped into treatment position on the Sonalleve table while they are awake. We position the lesion directly over the transducer, having first placed a gel pad between the membrane and the skin. We then image to make sure we're happy with the patient's position before we administer conscious sedation.

Delivering treatment

Each element of the ultrasound treatment (sonication cell) is delivered separately for a duration of between 16 and 55 seconds, depending on the power and size of the cell. At the same time a temperature mapping MR sequence is run to check where the heat is building up. This is important because the actual shape of the treatment cell areas can vary from what we planned, depending on the acoustic properties of the surrounding tissues.

For example in bone, an intact cortex reflects the ultrasound but we can exploit that to build up the heating where we want it – at the periosteum.

This temperature mapping in the soft tissues around the bone enables us to see how effective each sonification has been before moving on to the next one; or indeed terminating straight away if heat builds up where we don't want it. A cooling period of several minutes between each sonication avoids heat build-up in tissues outside the focus.

Post-treatment

Immediate MR imaging takes place, while the patient is still in the treatment position. A physical examination includes checking the skin, and the patient will be seen by a pain specialist on the ward before they are discharged. Patients are asked to keep a daily pain diary for 30 days at home. We contact them at days 7 and 14 to do questionnaires, and invite them back in at day 30 to do more imaging and a physical examination. This is repeated at day 60 and day 90 if they are willing.

Case study

A 51-year-old woman with metastatic breast cancer. Treated June 2014. Despite previous radiotherapy, shoulder pain remained uncontrolled by analgesia which severely restricted movements in her right arm. She was unable to carry out basic functions such as opening cupboards, putting on a seatbelt, and dressing herself.

Baseline imaging showed a well-defined focal lesion in the humeral head at the insertion of the infraspinatus tendon. There was also a more diffuse area of disease that extended further down the humerus.

This patient's treatment was delivered as 11 separate sonications of 3 x 4mm cells to 20.01.15 MRv3 cover the small focal lesion and 8 x 8mm cells to cover the more diffuse area. Power levels were quite low, ranging from 20-60W, in part because the lesion was quite superficial, but also because we were already seeing good heating at that level. The treatment time, including cooling periods, was 1 hour – plus set up and coming off the table time. The patient was discharged after two hours.

This patient has completed the study (90 days) with a good outcome. Her pain score had reduced to less than half the baseline by day 30 with huge increase in mobility of her arm to perform basic functions. At day 90 she reported a pain score of 0 at rest as well as at maximum abduction. .

Conclusion

So far we have seen successful outcomes in the first patients treated at The Royal Marsden and are recruiting further candidates for the trial. We are carrying out a huge amount of additional study, to develop better sequences in planning and monitoring our treatments, as well as pre-clinical, quality assurance and calibration work. Our enthusiastic multi-disciplinary team is now keen to expand into new clinical applications in patients who have exhausted other treatment options.

Brain Tumour Research reaches important milestone

Brain Tumour Research
Funding the fight

Neurosurgeon Kevin O'Neill who leads the new Brain Tumour Research Centre of Exellence.

The charity Brain Tumour Research has reached an important landmark with the opening of a new research centre in London.

The launch of a ground-breaking partnership with Imperial College Healthcare NHS Trust (London) means the charity is more than half-way towards its aim of creating a network of seven dedicated research centres.

Patients, carers, scientists, clinicians and charities from across the UK gathered at the Burlington Danes building adjacent to Hammersmith Hospital, for the official launch of the Centre of Excellence on 24th September. It joins centres at Queen Mary University of London, and at universities in Portsmouth and Plymouth, to become the fourth funded by Brain Tumour Research.

The charity's Chief Executive, Sue Farrington Smith, said: "This new centre brings a welcome and timely boost to long-term sustainable and continuous research into brain tumours. It is also a great milestone as it signifies we are more than half-way on our journey to create seven dedicated research centres. This number will ensure there is a critical mass of researchers who will bring us closer to a cure. With the assistance of our supporters and member charities, we will continue to work on behalf of the 16,000 people who are diagnosed with a brain tumour each year in order to fund the fight.

"Brain tumours kill more children and adults under the age of 40 than any other cancer ... yet just 1% of the national spend on cancer research is allocated to this devastating disease. This is unacceptable!"

The new centre was chosen after a rigorous selection process including international peer review. While existing centres are led by neuroscientists, Imperial College Healthcare NHS Trust's is the first in the charity's network to be headed up by a pioneering brain surgeon, Kevin O'Neill.

Earlier this year Mr O'Neill, consultant neurosurgeon at Imperial College Healthcare NHS Trust's Charing Cross Hospital, was part of a team who used an "intelligent" knife – or iKnife to diagnose abnormal tissue during an operation to remove a brain tumour. It was the first time it had been used in Europe.

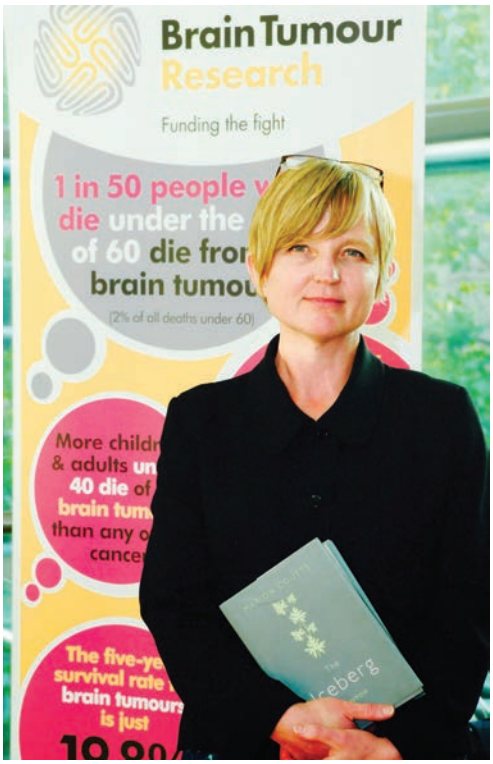
Mr O'Neill was consultant to John Fulcher who was lost to a glioblastoma multiforme (GBM) in June 2001 at the age of 52. John's widow Wendy went on to set up the Brain Tumour Research Campaign (BTRC) and is now chairman of Brain Tumour Research.

"John and I had been married for 16 years," said Wendy, 63, from West London. "When John was ill and after his death I learnt how little was known about brain tumours and how little research funding was available. Brain tumour research was seriously under-funded and I was shocked to learn there was no national charity dedicated to this area.

"There was nothing Kevin or I could do to save John but by launching my own charity and later becoming chair of trustees at Brain Tumour Research, I felt perhaps some good might come from bad – and it is helping Kevin and others who are able to tackle the terrible effects of the disease, and save others from the suffering that John and so many others have endured," she said.

Mr O'Neill said: "I continue to be astounded by the courage of patients and their families, none more so than in the case of Wendy who, in her grief, has found great depths of drive and determination

Wendy Fulcher with Kevin O'Neill placing a tile dedicated to her husband onto the "Wall of Hope'.



Marion Coutts.

to ensure our work has a future. We must fight this disease until we have a cure and we remain committed to doing all we can to improve outcomes for our patients.

"As a brain surgeon, it's my job to go in and remove brain tumours, but I know all too well that this isn't enough to remove the cancer. Working with a team of researchers, we are exploring novel treatments to halt brain tumour cell invasion into healthy brain tissue.

"I am delighted to be working with Brain Tumour Research to help push forward scientific frontiers to bring us closer to a cure."

Among those who attended the event was author Marion Coutts, who read an extract from *The Iceberg*, which won The Wellcome Book Prize 2015 and is a memoir about the diagnosis, illness and death of her husband, the art critic Tom Lubbock who died of a brain tumour in January 2011.

The research and fundraising partnership between Brain Tumour Research and the Trust aims to raise £1 million a year towards new studies involving clinicians at the Trust's neuro-oncology unit at Charing Cross Hospital working with scientists from Imperial College London.

The occasion also saw the unveiling of a new "Wall of Hope". Each day of research costs £2,740 and is represented by unique tiles on the wall which are dedicated to patients, their families, friends and corporate supporters.

The new centre is the second in London. Last year saw the opening of the Brain Tumour Research Centre of Excellence at Queen Mary University of London. Research here is focused on GBM and is led by Professor Silvia Marino, a leading brain tumour scientist and neuropathologist working within Queen Mary's Blizard Institute.

Also opened in 2014, the Brain Tumour Research Centre of Excellence at Plymouth University sits within the Peninsula Schools of Medicine and Dentistry. The team here, led by Professor Oliver Hanemann has a world-leading track record in researching low-grade brain tumours occurring in teenagers and adults. By identifying and understanding the mechanism that makes a cell become cancerous, the team explores ways in which to halt or reverse that mechanism. A key innovation is fast track: testing new drugs in human primary cell cultures leading to innovative phase 0 trials leading to adaptive phase II/III trials with the potential for making drug therapies available to patients both safely and faster.

The charity's first centre was established at the University of Portsmouth in 2009 and is now the largest dedicated brain tumour research centre in the UK under the leadership of Professor Geoff Pilkington. The centre has five research sub-groups which address different areas of brain tumour biology critical to the provision of knowledge which will underpin patient outcomes: childhood brain tumours, blood brain barrier (cancer metastasis and drug delivery), novel and re-purposed therapeutics, mitochondria and metabolism and tumour micro-environment.

Fundraising in its own right, Brain Tumour Research is also an umbrella charity, working in collaboration with member charities around the UK. Together with this network and supported by the fundraising achievements of Umbrella Groups and fundraisers across the UK, some £4 million was raised in 2014 to fund both brain tumour research and to provide support for patients and families. The charity is striving to fund a network of seven dedicated research centres whilst challenging the government and larger cancer charities to invest more in brain tumour research.

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Contraindications: Hypersensitivity to the active substance or porphyrins; acute or chronic types of porphyria; pregnancy.
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Substance-specific side effects: *Uncommon:* Hypotension; nausea, photosensitivity reaction, photodermatosis.
Substance-specific side effects: *Uncommon:* Hypotension; nausea, photosensitivity reaction, photodermatosis.
Procedure-related side effects: The extent and frequency of procedure-related neurological side effects depend on the localisation of the brain tumour and the degree of resection of tumour tissue lying in eloquent brain areas. *Very common:* Anaemia, thrombocytopenia, leukocytosis. Blood bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase or blood amylase increased. *Common:* Neurological disorders (e.g. hemiparesis, aphasia, convulsions, hemianopsia). Thromboembolism. Vomiting, nausea. *Uncommon:* Brain oedema, hypotension. *Very rare:* Hypesthesia; diarrhoea. One case of moderate chills; one respiratory insufficiency after overdose, which resolved completely.
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The clinical and scientific team members at the new Imperial College Brain Tumour Research Centre of Excellence

Clinical

Mr Kevin O'Neill is Head of Neurosurgery and Honorary Senior Lecturer in the Division of Brain Sciences, Department of Medicine, Imperial College London and now directs the new Brain Tumour Research Centre of Excellence at Imperial College London.

Kevin is a Consultant Neurosurgeon, Head of Neurosurgery and Trust lead for Neuro-oncology at Imperial College Healthcare NHS Trust specialising in neurosurgical oncology and complex neurovascular surgery. He also leads the Neuro-oncology research group at Imperial College and its various collaborations internally, nationally and internationally. Over and above his medical practice, he chairs the Board of Trustees for the Brain Tumour Research Campaign a founder member of the charity Brain Tumour Research. More generally he is the National Institute of Healthcare Research (NIHR) Specialty Lead for Cancer in The North West London Clinical Research Network and sits on the Clinical Pathway Group for Brain and CNS cancer for the London Cancer Alliance (LCA) integrated cancer network.

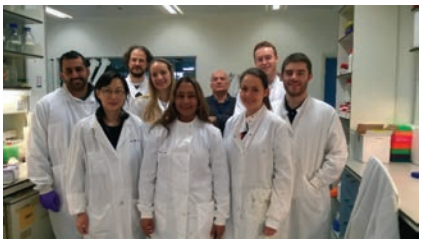
During his early career in neurosurgery Kevin also experienced the value of a working brain tumour research lab by spending time in Prof. Geoff Pilkington's laboratories at King's College London where he was engaged in work on the cell adhesion molecule receptor, CD44 in glioma. This appreciation of lab science has led to the development of a team of world-class researchers to investigate the biology of tumour metabolisms to further understand the behaviour of this disease. Moreover, the clinical team will also be able to extend their use of innovative 3D real time surgical imaging. Earlier this year and along with Mr Babar Vaqas, he used Raman Spectroscopy to diagnose abnormal tissue during an operation to remove a brain tumour; the first time such technology had been used in Europe.

Dr Matt Williams is Consultant Clinical Oncologist and Honorary Clinical Senior Lecturer at Imperial. Matt has a clinical and research interest in brain and central nervous system tumours. Clinically, he delivers radiotherapy and chemotherapy to patients with brain and spinal tumours, including Intensity Modulated Radiation Therapy and stereotactic radiotherapy.

His clinical research focuses on patterns of care and outcomes in patients with a wide range of tumours, and developing better ways of assessing patient outcomes. From a scientific perspective, he is interested in the application of novel scientific and computational techniques to clinical problems. These include novel techniques for systemic reviews and evidence aggregation as well as mathematical modelling of prognosis in patients receiving palliative chemotherapy.

Matt works mainly at Charing Cross Hospital, with an excellent multi-disciplinary team of surgeons, radiologists, nurses, oncologists and others who provide diagnostic and treatment services across, and beyond, north-west London. The most recent National Cancer Intelligence Network data shows that the team have the best brain tumour survival in the country.

Scientific Research



The primary aim of the research team is to use genetic, epigenetic and metabolomic approaches to identify the key molecular events underpinning development of Glioblastoma Multiforme (GBM); the most aggressive and lethal primary brain tumour. Cancer is increasingly recognised as a disease underpinned by profound changes in cellular metabolism. This altered metabolism represents cancer's achilles' heel and our key questions are based around identifying and testing these metabolic changes to determine if they would be novel therapeutic strategies for GBM. Moreover, since tumour hypoxia (low 0_2 levels) constitutes a major challenge to current cancer therapies, they are investigating gene regulation and expression under such physiologically relevant conditions.

They envisage that their comprehensive approach will reveal cancer specific altered pathways and identify new therapeutic strategies for brain tumours.

Dr Nelofer Syed is Principle Investigator of the John Fulcher Molecular Neuro-oncology Laboratory at Imperial College.

Dr Syed obtained her PhD in Molecular Immunology from Imperial College under the direction of Professor Margaret Dallman. After her PhD training she pursued her interests in translational cancer epigenetics at the Ludwig Institute of Cancer Research, London. Her main focus here centred on identifying cancer specific epigenetic changes that could be targets for therapy. She continued her research at the Institute of Cancer Research, London, where she played a key role in identifying a gene (Tip60) having a critical involvement in breast cancer development.

In 2009 she returned to Imperial College to set up the John Fulcher Molecular Neuro-oncology Laboratory funded by the Brain Tumour Research Campaign (BTRC). Her programme of research investigates various aspects of brain tumour biology, genetics and epigenetics with a particular emphasis on identifying altered metabolic pathways to devise novel therapeutic strategies. Her lab has already generated

novel data on deranged amino acid metabolism that she believes will form the basis of a phase 2 clinical trial of arginine depletion as a novel therapeutic strategy for brain tumours.

Mr Babar Vaqas is a Neurosurgeon and Research Fellow at the Imperial College Healthcare NHS Trust.

Mr Vaqas is carrying out two cutting edge studies looking at new ways of diagnosing tumour tissue during surgery. Together with Mr O'Neill he is leading the first application of the iKnife system during Neurosurgery in the world. Earlier this year he used a laser probe to diagnose abnormal tissue during an operation to remove a brain tumour. This was the first time the technology had been used in Europe.

His post as a neurosurgeon is supported by the Pickard Foundation and the project is supported by Brain Tumour Research Campaign (BTRC) and Brain Tumour Research (BTR). Mr Vaqas obtained his medical degree from the University of Oxford and completed basic surgical training in Cambridge.

Dr Matthew Grech-Sollars is a Research Associate in MRI physics working in the field of Neuro-Oncology Neuroimaging with Dr Adam Waldman. His key interest is in developing novel imaging techniques, with a particular focus on MRI, to improve clinical outcomes for patients with brain tumours, and a vision of having these methods integrated into clinical practice.

Matthew joined Imperial College London in 2014, after receiving his PhD from University College London, titled "Diffusion MRI for characterising childhood brain tumours" and supervised by Prof Chris A Clark. Previously, he obtained his MSc in Biomedical Engineering with Medical Physics from Imperial College London in 2010, after having worked in industry as an Engineer for three years.

Dr Fernando Abaitua has been a Postdoctoral Research Associate since 2013 in Dr Syed's group at the molecular neuro-oncology John Fulcher Molecular laboratory, funded by BTRC, and is involved in multiple projects tackling epigenetic differences in cancer metabolism of the most aggressive form of brain tumours, glioblastoma multiforme. His projects are focused on the cellular and molecular mechanisms behind arginine deprivation and the role of collagen-prolyl hydroxylases in glioma biology, in the context of primary cell lines and isolated tumour stem cells under physiological oxygen conditions.

Dr Combiz Khozoie, a Postdoctoral Fellow and **Alexander Renziehausen**, a PhD student are currently funded by the Barrow Neurological Foundation UK, a UK charity based in London that acts as the international fund-raising and education arm of the world-renowned Barrow Neurological Institute (BNI) in Phoenix, Arizona. **Julia Langer** is supported by a Grassini PhD studentship through BTRC, she is currently in the process of writing up her thesis. **John DeFelice** joined BTRC in 2011 as lab manager. The newest recruits include **Richard Perryman**, an MRC funded PhD student and **Dr Tzouliana Stylianou**, a BTRC funded postdoctoral fellow.

MANAGING OPIOID-INDUCED CONSTIPATION IN ADULT CANCER PATIENTS

Dr Andrew Davies, Clinical Director Supportive & Palliative Care, Royal Surrey County Hospital / St. Luke's Cancer Centre

Constipation is the most common adverse effect experienced by patients receiving opioid analgesics ("opioid-induced constipation / OIC").[1] OIC has been defined as "a change when initiating opioid therapy from baseline bowel habits that is characterised by any of the following: a) reduced bowel movement frequency; b) development or worsening of straining to pass bowel movements; c) a sense of incomplete rectal evacuation; and d) harder stool consistency.[2]

OIC has a unique pathophysiology, which explains its relative resistance to conventional laxatives.[2] Opioids act on mu-opioid receptors in the gastro-intestinal tract[3] and cause decreased small and large bowel motility, decreased secretion of fluid into the small bowel, increased absorption of fluid from the small and large bowel, increased tone in sphincters, and reduced ano-rectal sensitivity.[3] OIC is a problem with all opioid analgesics, and there is no good evidence of a dose response relationship.

The management of constipation involves both non-pharmacological interventions (e.g. diet, exercise), and pharmacological interventions (e.g. conventional laxatives, targeted therapies). Patients with OIC should be encouraged to eat a healthy diet, maintain hydration, and exercise appropriately, although there is no evidence that these interventions are effective in managing OIC. Guidelines recommend prescribing prophylactic conventional laxatives to patients commencing opioid analgesics, and often the use of a softener and a stimulant laxative.[4] Again, there is little evidence that conventional laxatives are effective in managing OIC.[2] Other pharmacological interventions that have been investigated in OIC include lubiprostone (a chloride channel activator), and a variety of so-called peripherally acting mu-opioid receptor antagonists (PAMORAs).[2] The rationale for using PAMORAs is that they target the underlying pathophysiology.[3] Subcutaneous methylnaltrexone has been available for a number of years, and the evidence suggests that it is very effective, and is generally well tolerated.[3]

Recently, oral naloxegol (Moventig®▼; AstraZeneca) has been licensed for the treatment of opioid-induced constipation (OIC) in adult patients who have had an inadequate response to laxative(s).[5] Naloxegol is a once a day, oral preparation, which has a gentle onset of action: the median time to laxation in the pivotal clinical studies was 6-12 hours.[5] Naloxegol is effective in patients that have not responded to conventional laxatives, and the response was sustained in a subsequent long term follow up study.[6] In July 2015, the National Institute for Health and Care Excellence (NICE) published a technology appraisal guidance for naloxegol.[7] The guidance states that naloxegol is recommended "as an option for treating opioid induced constipation in adults whose constipation has not adequately responded to laxatives"[7], and irrespective of the underlying cause of pain (i.e. cancer*, non-cancer). Naloxegol is contraindicated in patients with gastro-intestinal obstruction, and patients at heightened risk of gastro-intestinal perforation.[5] Prescribers should consult the summary of product characteristics before prescribing naloxegol.

*There is limited clinical experience of Moventig® in OIC adult patients with cancer related pain.[7]

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PRESCRIBING INFORMATION

MOVENTIG®▼12.5mg and 25mg film-coated tablets (naloxegol oxalate). Consult Summary of Product Characteristics before prescribing. **Use: Adults:** treatment of opioid-induced constipation (OIC) in adult patients who have had an inadequate response to laxative(s). For definition of inadequate response to laxative(s), refer to section 5.1 of SmPC. **Presentation:** 12.5mg or 25mg naloxegol film-coated tablet. Dosage and administration: Recommended 25mg once daily. Take on empty stomach at least 30 minutes prior to first meal of day or 2 hours after first meal of day. Elderly patients (≥65 years): No adjustment recommended. **Renal impairment:** Moderate to severe renal impairment starting dose 12.5mg. Discontinue if side effects impact tolerability. Increase to 25mg if well tolerated. No adjustment required for mild renal impairment. Hepatic impairment: No adjustment required in mild to moderate impairment. Use in severe hepatic impairment not recommended. Moderate CYP3A4 inhibitors: Starting dose 12.5mg, can be increased to 25mg if well tolerated. No adjustment required for weak CYP3A4 inhibitors. Cancer-related pain: No adjustment required. Paediatric population (<18 years): Safety and efficacy not yet established. **Contraindications:** Hypersensitivity to active substance or any of the excipients or any other opioid antagonist. Patients with known or suspected gastrointestinal (GI) obstruction or patients at increased risk of recurrent obstruction. Patients with underlying cancer who are at heightened risk of GI perforation, such as those with underlying malignancies of gastrointestinal tract or peritoneum, recurrent or advanced ovarian cancer, vascular endothelial growth factor (VEGF) inhibitor treatment. Concomitant use with strong CYP3A4 inhibitors (e.g. clarithromycin, ketoconazole, itraconazole or telithromycin; protease inhibitors such as ritonavir, indinavir or saquinavir; grapefruit juice when consumed in large quantities). **Warnings and precautions:** Use with caution in patients with any condition which might result in impaired integrity of the gastrointestinal tract wall. Advise patient to discontinue therapy and promptly notify physician if unusually severe or persistent abdominal pain develops. Use with caution in patients with clinically important disruptions to the blood brain barrier with observation for potential CNS effects. Discontinue if evidence of opioid-mediated interference with analgesia or opioid withdrawal syndrome occurs. Use with caution in patients taking methadone. Cases of opioid withdrawal syndrome have been reported in the naloxegol clinical programme (DSM-5). If opioid withdrawal syndrome is suspected the patient should discontinue Moventig and contact their physician. Use with caution in patients 6 months following myocardial infarction, symptomatic congestive heart failure, overt cardiovascular (CV) disease or patients with a QT interval of ≥500msec. Use with caution in OIC patients with cancer-related pain. **Drug interactions:** Strong CYP3A4 inducers: Concomitant use not recommended. P-gp inhibitors: Dosing recommendations for Moventig when co-administered with medicinal products causing both P-gp and CYP3A4 inhibition should be based on CYP3A4 inhibitor status – strong, moderate or weak. Fertility, pregnancy and lactation: Not recommended during pregnancy or breast-feeding. The effect of naloxegol on fertility in humans has not been studied. **Undesirable events:** Consult SmPC for full list of side effects. Very Common: Abdominal pain, diarrhoea. **Common:** Nasopharyngitis, headache, flatulence, nausea, vomiting, hyperhidrosis. **Uncommon:** Opioid withdrawal syndrome. **Legal category:** POM. **Marketing authorisation number:** Moventig 12.5mg film-coated tablets 30 EU/1/14/962/001; Moventig 25mg film-coated tablets 30 EU/1/14/962/005. **Basic NHS cost:** Moventig 12.5mg film-coated tablets 30; £55.20; Moventig 25mg film-coated tablets 30; £55.20. **Marketing Authorisation holder:** AstraZeneca AB, SE-151 85 Södertälje, Sweden. **Further information is available from:** AstraZeneca UK Ltd., 600 Capability Green, Luton, LU1 3LU, UK. Moventig is a trade mark of the AstraZeneca group of companies. **Date of preparation:** 08/2015. PAI 15 0001

ATLAS ID: 899,725.011 Date of preparation: September 2015

moventig®▼ naloxegol

Clinical strategies for chemoprevention of breast cancer (Part 2)

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This is the second of a two part article on chemoprevention which will focus on national and international guidelines for chemoprevention of breast cancer and consider optimal approaches to maximise uptake and benefit from potential reductions in breast cancer incidence.

Assessment of breast cancer risk

Chemoprevention should only target women at substantially elevated risk of developing breast cancer. This includes all women aged 35 years or older with a breast cancer risk ≥1.66% in the next five years, based on the Gail Model or those with lobular carcinoma in situ (LCIS) [1]. Several societies and organisations have evaluated the evidence for chemoprevention and endorsed its implementation, including the American Society of Clinical Oncology (ASCO) [2], United States Preventive Services Task Force (USPSTF) [3] and the National Comprehensive Cancer Network [4]. Most consider a Gail Model risk score of at least 1.66% to be an appropriate level of risk for chemoprevention, and the National Cancer Institute has developed a risk assessment tool for identification of women at increased risk [www.cancer.gov/bcrisktool]. Freedman and colleagues employed a retrospective analysis to compile risk tables incorporating not only conventional risk assessment data, but factors such as age, race, ethnicity and uterine status [5]. Based on these amended risk estimations, the USPSTF have recently suggested that the risk:benefit calculation for women aged over 50 years favours a five-year risk of 3%, greater than the present norm of 1.66% [3]. All chemotherapeutic agents have some level of adverse side-effects and the risk:benefit ratio in the chemopreventive setting is more delicate when these agents are administered to otherwise healthy women where there is no measurable biomarker to act as a predictor of efficacy (c.f. statins and LDL levels). Post-menopausal women are more susceptible to side-effects of chemopreventive agents, namely SERMS. Tools for risk assessment in the United Kingdom differ from the United States where the Gail model is popular and based on five key factors – current age, age at first live birth, age at menarche, number of first degree relatives with breast cancer and benign breast biopsies [1]. Other instruments for risk assessment of proven clinical value include Tyrer-Cuzik [6] and the Manchester scoring system [7]. Tyrer-Cuzik is a user-friendly web-based model that includes a more detailed family history, as well as body mass index and LCIS. Genetic testing is now being offered to women with a strong family history of breast cancer when the combined BRCA1/BRCA2 carrier probably is ≥10% rather than the previous threshold of 20%.

Recommendations for chemoprevention based on current guidelines

ASCO published updated guidelines on use of pharmacological interventions for breast cancer reduction in July 2013 [2]. These represented a watershed in chemoprevention as the phrase 'may be offered' was replaced with 'should be discussed as an option', thereby implying some incumbency on the part of clinicians to consider chemoprevention as a management option for higher risk women. Thus tamoxifen (20mg per day orally for five years) should be discussed as an option to reduce the risk of oestrogen receptor-positive invasive breast cancer in premenopausal and postmenopausal women, whereas a similar recommendation applies to raloxifene (60mg per day orally for five years) for postmenopausal women only. Furthermore, these most recent updates acknowledge the aromatase inhibitor, exemestane (25mg per day orally for five years), as an additional option for breast cancer risk reduction in postmenopausal women (ER-positive disease only). These recommendations apply to women aged ≥35 years with an estimated five-year risk of breast cancer of 1.66 based on the aforementioned NCI risk assessment tool, but not to those with a personal history of breast cancer or a known BRCA gene mutation. It should be noted that no trials have specifically examined the effect of chemoprevention in mutation carriers, although trials of high risk groups would inevitably include some mutation carriers who may also be more susceptible to the teratogenic effects of tamoxifen. The USPSTF concur with these key recommendations, but have suggested that a five-year risk for invasive breast cancer of 3% may ensure that women derive greater benefit than harm from pharmacological intervention for risk reduction [3]. Ultimately all women must individually discuss risk and benefits with healthcare professionals prior to making a final decision. Exemestane is an appropriate agent for higher risk women who have a history of deep vein thrombosis, pulmonary embolus, stroke,

Table 1: Recommendations for chemoprevention in higher risk women		
	PRE-MENOPAUSAL WOMEN	POST-MENOPAUSAL WOMEN
USA	TAMOXIFEN * (20mg daily for 5 years)	TAMOXIFEN * (20mg daily for 5 years)
		RALOXIFENE** (60mg daily for 5 years)
		EXEMESTANE (25mg daily for 5 years)
UK	TAMOXIFEN* (20mg daily for 5 years)	TAMOXIFEN * (20mg daily for 5 years)
		RALOXIFENE** (60mg daily for 5 years)
* – no significantly increased risk of endometrial cancer or blood clots ** – no significantly increased risk of endometrial cancer [tamoxifen, raloxifene and exemestane taken as oral preparations]		

transient ischaemic attack or current prolonged immobilisation. Moreover, exemestane might be considered to lower the risk of contralateral disease in women who have undergone unilateral mastectomy for diffuse DCIS. These chemopreventive agents should not be combined with HRT, although this was permitted in the IBIS-1 trial [8].

The National Institute for Health and Care Excellence (NICE) recommends offering tamoxifen and raloxifene (as above) to high risk (>30%) postmenopausal women and considering chemoprevention in moderate risk (>17%; <30%) women with no personal history of breast cancer (Table 1). This excludes those women without a uterus who have a past history of endometrial cancer or an intact uterus and risk of thromboembolic or endometrial cancer. Tamoxifen can also be offered to premenopausal women ≥35 years and the overall reduction in breast cancer incidence is calculated to be 3% (or 408,000 women in the UK population) [8].

Uptake of chemoprevention among at risk women

Thus far, uptake of chemoprevention strategies in the United States (where tamoxifen has been licensed for this use for over a decade) has been low, with a survey conducted in 2010 indicating that <1% of women were using tamoxifen or raloxifene for breast cancer prevention [9]. There is a need for healthcare professionals to promote this method of cancer prevention as the magnitude of risk reduction is substantial for some women who may also be at low risk of adverse side-effects. Tamoxifen is associated particularly with thromboembolism and uterine cancer, but these are not shared by either raloxifene or aromatase inhibitors. Furthermore, side-effects reported in recent trials of aromatase inhibitors in the chemopreventive setting are not severe, with no major adverse events in the MAP3 trial and only minimal impairment of health-related quality of life [11]. Despite this new directive from professional organisations, the United States Food and Drug Administration (FDA) has not approved any aromatase inhibitors for reduction of breast cancer risk. Neither tamoxifen nor raloxifene are licenced as chemopreventive agents in Europe. There is probably a need for better education of patients and healthcare workers about the risk:benefit for chemoprevention, with shared decision-making that incorporates a woman's personal values and preferences.

Combining SERMS and aromatase inhibitors for chemoprevention

Hitherto, trials of aromatase inhibitors as chemopreventive agents have compared one of these agents against a placebo rather than a head-to-head comparison with another chemopreventive agent. NICE have emphasised that there are no randomised controlled trials comparing tamoxifen or raloxifene (SERM) with an aromatase inhibitor. It would seem sensible to undertake a randomised comparison of an aromatase inhibitor (anastrozole, letrozole or exemestane) with either tamoxifen or raloxifene, which could better inform women about the best approach for chemoprevention of breast cancer. Raloxifene has much attenuated ureterotrophic activity and is probably a more appropriate agent for any direct head-to-head comparison with an aromatase inhibitor. Randomised, controlled trials have shown benefit in disease-free survival in postmenopausal women receiving aromatase inhibitors as adjuvant therapy. The oral aromatase inhibitors, anastrozole, letrozole and exemestane, are of comparable anti-tumour efficacy and are potentially interchangeable. Longer term data for side effect profiles and toxicities must be awaited before definitive recommendations on clinical use.

The most appropriate sequencing with or without tamoxifen, long-term toxicity, and any overall survival benefit for adjuvant treatment with aromatase inhibitors have yet to be determined. A recent patient-level meta-analysis examined randomised trials of five years of tamoxifen versus continuous aromatase inhibition, or sequenced with an aromatase inhibitor for a total duration of five years. On average, for postmenopausal breast cancer a switch strategy incorporating an aromatase inhibitor significantly reduced recurrence (RR 0.56 in years two to four; 0.97 after five years) and fewer deaths (RR 0.84) compared with 5 years of tamoxifen monotherapy. There were more fractures (RR 1.40) in patients receiving aromatase inhibitors but fewer cases of endometrial cancer (RR 0.37) [12].

In the chemopreventive setting, there may be advantages of using an early switch policy in terms of maintaining bone health and minimising musculoskeletal symptoms (which can be a nuisance to women who are otherwise fully healthy). Patient-reported outcomes from the STAR trial showed that those treated with raloxifene experienced more musculoskeletal symptoms, weight gain and dyspareunia, whereas patients treated with tamoxifen had more vasomotor symptoms, leg cramps, and bladder control problems and gynaecologic problems [13]. An optimal trial design for chemoprevention of breast cancer might be an aromatase inhibitor after initial therapy with tamoxifen or raloxifene for two to three years, for which there is some biological rationale. Thus hormone-dependent breast cancer cells in vitro develop oestrogen hypersensitivity and upregulation of aromatase when grown in oestrogen poor media, whereas in animal models there is initial regression of tumours in response to tamoxifen, but subsequent stimulation by the agonist component of this SERM. Therefore sequential administration of an aromatase inhibitor would be a logical approach as these agents would both negate the

oestrogen agonist effect of tamoxifen, and reduce local and circulating levels of oestrogen. It remains unclear whether any early switch sequence with a SERM and aromatase inhibitor would be associated with a 'carry-over' effect, as witnessed for tamoxifen (and raloxifene) whereby the benefits continue beyond the treatment period. The duration of follow-up should be a minimum of 10 years in order to identify potential longer term sequelae of interventions with agents that induce hypoestrogenic states which affects bone mineral density, cardiovascular deaths (elevated cholesterol) and neurocognitive function. There is no evidence to date of any reduction in mortality from chemoprevention strategies, and breast cancer specific/overall survival will be important outcomes to measure.

Conclusions

The development of a SERM that combines risk reduction for breast cancer with incidental benefits in other tissues may be a more promising approach to chemoprevention than aromatase inhibitors, which induce a hypoestrogenic state that could be associated with more intense adverse sequelae in the longer term. Newer SERMs have shown promising results with favourable risk:benefit ratios (namely absence of thromboembolic events and uterotrophic effects). A combination using a SERM and aromatase inhibitor sequentially for chemoprevention might be an optimal strategy at the present time and maximise cost-effectiveness with least side-effects. Furthermore, a single pulse of treatment for five years has been advocated for chemoprevention, but this recommendation is based to some extent on concerns about the longer-term stimulatory effects of tamoxifen. Aromatase inhibitors may be potential candidates for longer chemoprevention, notwithstanding issues of safety and quality of life relating to oestrogen deprivation. Further clinical trials are essential to evaluate aromatase inhibitors as chemopreventive agents in high risk postmenopausal women. These agents are associated with a greater reduction of contralateral breast cancer in adjuvant trials than tamoxifen, and are not associated with increased risks of thromboembolism or uterine malignancy. Nonetheless, follow-up is mandatory to determine longer term effects on bone mineral density and musculoskeletal symptoms, as well as cognitive function. Aromatase inhibitors could potentially be combined with a gonadotrophin releasing hormone agonist as a chemopreventive strategy in premenopausal women, but there are concerns about side effects of profound oestrogen deprivation and the optimum duration of therapy is unknown.

It is important to take account not only of the clinical efficacy of individual agents and their potential to reduce both incidence and mortality of breast cancer, but the selection of patients at greatest risk who are least susceptible to the adverse sequelae of pharmacological intervention. New approaches for communication of risk must be developed that are commensurate with race, ethnicity and levels of educational attainment. Ultimately, an ideal chemopreventive strategy will target the most appropriate "at risk" groups with the most effective agents that can be monitored with biomarkers and administered for a finite period of time with minimum side-effects and at low cost (Figure 1).

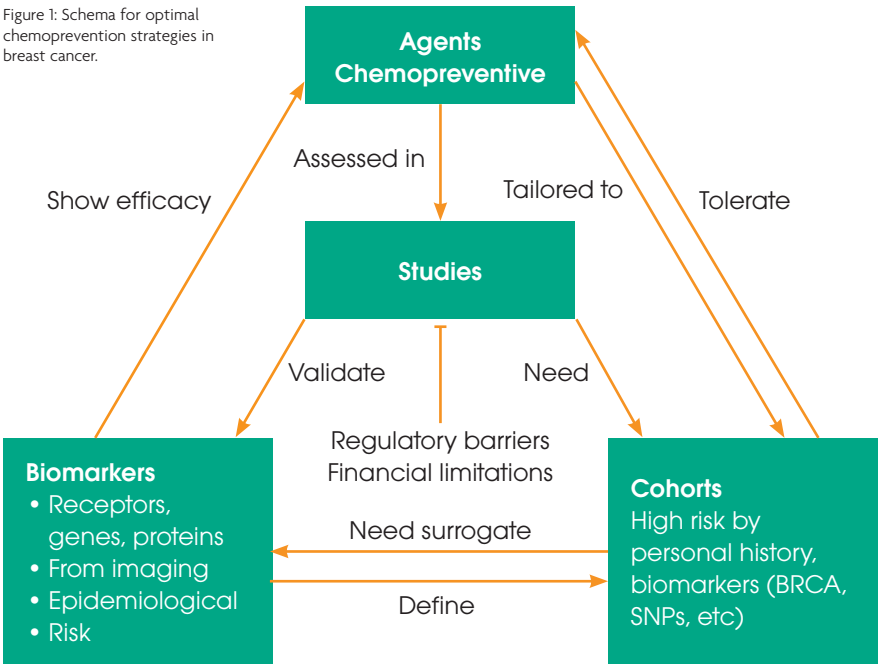

Figure 1: Schema for optimal chemoprevention strategies in breast cancer.

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A systemic abscopal effect following localised palliative radiotherapy for metastatic leiomyosarcoma

Case Report

An 84-year old woman presented to the sarcoma service at the Leicester Royal Infirmary with a two-year history of swelling in the left posterior thigh. This had been gradually enlarging until it became painful, at which point she sought the attention of her General Practitioner who referred her to the sarcoma service. An MRI scan in August 2013 detected multiple lesions in the left posterior thigh bridging the posterior compartment and extending into the subcutaneous tissues, the largest measuring 9cm in length by 6cm in depth by 7cm in coronal width. Multiple solid cellular areas were noted with areas of necrosis along the deep margin. A provisional radiological diagnosis of a sarcoma was made and the patient underwent CT scanning of the chest, abdomen and pelvis in September 2013 as part of staging investigations. The CT (Figure 1) showed multiple (at least seven, two of which are demonstrated in figure 1) soft tissue nodules within the lungs in keeping with metastatic deposits. A necrotic 9mm left pelvic side wall lymph node was also noted.

The patient underwent a CT-guided biopsy of the thigh mass, which was reported as good representative cores containing partly necrotic malignant tumour (Figure 3). The tumour was composed of sheets of pleomorphic cells which appeared plump spindled and epithelioid, admixed with inflammatory cells including conspicuous eosinophils. There were no lipoblasts and no obvious myxoid change to the stroma. The tumour showed patchy staining for one of the epithelial markers, AE1/3, together with patchy staining for Desmin. There was non-specific staining for CD31, but CD34 was negative. CAM 5.2, BP4, CK7, CK20, SMA, myogenin and S100 were all negative. CEA showed background non-specific staining.

The patient's radiology and histology were reviewed at the East Midlands Sarcoma Service regional multi-disciplinary meeting (MDT) and a consensus diagnosis of a high grade leiomyoscarcoma was made. Recommended treatment was palliative radiotherapy to the left thigh mass to improve symptoms, with a view to local resection if this was unsuccessful. The patient was referred to the local Clinical Oncologist who discussed a dose of 30Gy in 10 daily fractions over two weeks with the patient. This was delivered using two opposed 6MV photon beams arranged to cover the gross tumour volume with a 2cm margin, treating Monday to Friday at 3Gy per day. The patient tolerated her treatment well and was reviewed in clinic four weeks later. Note was made of a slight shrinkage of her tumour and the patient was experiencing some relief of her symptoms. Arrangements were made for a restaging CT scan to assess the progress of her presumed metastatic disease.

The repeat CT (Figure 2) in December 2013 demonstrated resolution of the lung nodules and improvement in the size of the pelvic side wall lymph node. The case was again discussed in the sarcoma MDT and the patient was referred for a repeat MRI scan of her left thigh prior to considering surgical excision. This showed an increase in size of the soft tissue mass, now measuring 12 x 8.5 x 6.7cm with no post-contrast enhancement. The patient underwent a wide local excision of her thigh lesion in January 2014, with the post-operative histology (Figure 4) showing the lesion to be necrotic throughout, with a surrounding rim of fibrosis incorporating large aggregates of macrophages. These changes extended to the deep fascia, but all other margins consisted of normal connective tissue. No viable tumour was seen

Figure 1: Initial CT Scan demonstrating multiple lung nodules (arrowed).

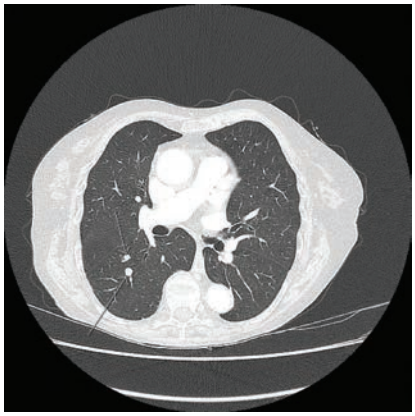
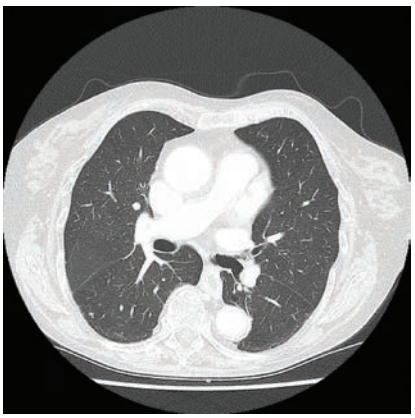


Figure 2: Repeat CT scan after palliative radiotherapy to thigh lesion.



despite extensive sampling.

The patient recovered well from her operation and was discharged home with the plan for a follow-up CT scan in three months to re-assess the previous areas of presumed metastatic disease. The patient has subsequently had two further CT scans in April and August 2014, which are clear of any radiological evidence of metastatic disease. She remains under clinical review every six months however further radiological and clinical examination has revealed no evidence of a local recurrence to date and the patient remains very well.

Discussion

The abscopal (derived from Latin 'ab' meaning "away from" and Greek 'skopós' meaning "target") effect is a well-recognised, but poorly understood, likely immune mediated phenomenon where localised treatment of a tumour by radiation or other localised treatment causes shrinkage of tumours at locations distant from the treated area. Such responses are rare [1], but cases have been reported for a variety of cancers, including melanoma, cutaneous lymphoma, adenocarcinoma of the lung and renal cell tumours. As far as the authors of this report are aware, there has been no reported case of an abscopal effect in high grade sarcoma in the literature.

This patient had radiological evidence of metastatic disease with multiple nodules seen throughout both lungs on the staging CT scan; however, we recognise that these lesions were not sampled and therefore metastatic disease was not histologically proven. The patient also had a 9mm necrotic left sided pelvic lymph node which went unsampled. The post-operative histology obtained from the thigh lesion is, however, compelling in that it demonstrates a clear immunologically mediated response with large aggregates of macrophages with no tumour seen despite extensive sampling.

The mechanism of how the abscopal effect occurs is poorly understood. It is hypothesised that by irradiating the tumour, this releases tumour antigens and promotes cytokine production, thus recruiting antigen presenting cells and invoking a systemic anti-tumour immune response; however there is little evidence to substantiate this. One previous case report of a patient with hepatocellular carcinoma [2] reported increased

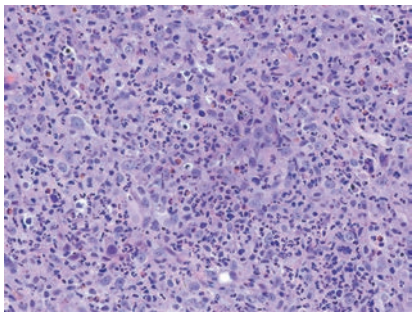


Figure 3: Pre-Radiotherapy histology (biopsy).

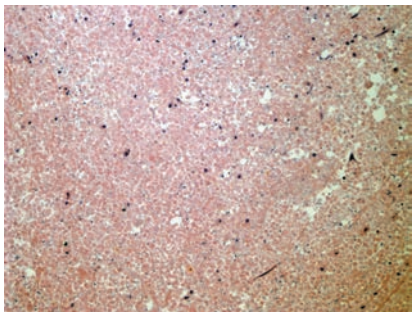


Figure 4: Post-surgical histology (excision).

circulating serum TNFÐ following radiotherapy of a bone metastasis, accompanied by a decrease in the size of the non-irradiated tumour. A further case report [3] of an abscopal effect in patient with metastatic melanoma demonstrated detectable post-radiation anti-melanoma antibodies, noting also that vitiligo can arise in non-irradiated skin after treating melanoma with radiation. This suggests an immune response to tumour melanocytes can also cross-react with normal melanocytes at distant sites [4].

Further trials have been conducted in different tumour sites to investigate if an immune response can be invoked after palliative radiotherapy. The results of a recent phase-3 trial investigating placebo vs ipilimumab after palliative radiotherapy for bone metastasis in prostate cancer have been published in the Lancet [5]. The authors found no significant difference in overall survival for either patient group, but did comment that the investigated drug did offer signs of activity that warranted further investigation. It is important to note, however, that there were 4 deaths within the ipilimumab group due to treatment toxicity (none in the placebo group).

It is also of interest to contrast the regression seen in cases of the abscopal effect with the diametric opposite – the reactivation of distant metastasis or even the detection of new metastatic disease. The suggested explanation of this mechanism, often reported by surgeons as well as radiation oncologists, is frequently attributed to the same anti-tumour immune mediated effects postulated as involved in the abscopal effect. Some authors may argue that this is due to low dose radiation leakage from machine heads or intrinsic radiation sensitivity. However the short period of latency of these effects would suggest otherwise. In the current radiotherapy age of IMRT/IGRT many clinicians are concerned about the effect of the low dose radiation bath these techniques expose the patient to and how this might impact on secondary cancer risk. Prostate cancer patients followed up 10 years after radiotherapy have a detectable increase in secondary malignancies at sites distant to their irradiated field compared to patients who did not receive radiotherapy [6].

In conclusion, radiotherapy has always traditionally been viewed as an effective local treatment modality, but there is clinical evidence now in multiple tumour sites of an effect extending beyond this. It is clear that the effects can be beneficial for some patients, but potentially harmful for others. The mechanisms involved are likely to be multifactorial and difficult to extricate from one another in each case. Further work is warranted in this area to improve our understanding of the immune processes involved so that potential targets can be incorporated into future clinical trials, hopefully expanding the involvement of the immune system in medium to long term control of patients with metastatic disease.

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Journal of Clinical Oncology

Prediction of serious complications in patients with seemingly stable febrile neutropenia: validation of the Clinical Index of Stable Febrile Neutropenia in a prospective cohort of patients from the FINITE study

Alberto Carmona-Bayonas A, Paula Jiménez-Fonseca, Juan Virizuela Echaburu, et al. Journal of Clinical Oncology 2015;Feb 10:465-47.

Purpose: To validate a prognostic score predicting major complications in patients with solid tumours and seemingly stable episodes of febrile neutropenia (FN). The definition of clinical stability implies the absence of organ dysfunction, abnormalities in vital signs, and major infections.

Patients and Methods: We developed the Clinical Index of Stable Febrile Neutropenia (CISNE), with six explanatory variables associated with serious complications: Eastern Cooperative Oncology Group performance status ≥2 (two points), chronic obstructive pulmonary disease (one point), chronic cardiovascular disease (one point), mucositis of grade ≥2 (National Cancer Institute Common Toxicity Criteria; one point), monocytes <200 per μL (one point), and stress-induced hyperglycemia (two points). We integrated these factors into a score ranging from zero to eight, which classifies patients into t3 prognostic classes: low (zero points), intermediate (one to two points), and high risk (≥3 points). We present a multicenter validation of CISNE.

Results: We prospectively recruited 1,133 patients with seemingly stable FN from 25 hospitals. Complication rates in the training and validation subsets, respectively, were 1.1% and 1.1% in low-, 6.1% and 6.2% in intermediate-, and 32.5% and 36% in high-risk patients. Mortality rates within each class were 0% in low-, 1.6% and 0% in intermediate-, and 4.3% and 3.1% in high-risk patients. Areas under the receiver operating characteristic curves in the validation subset were 0.652 (95% CI, 0.598 to 0.703) for Talcott, 0.721 (95% CI, 0.669 to 0.768) for Multinational Association for Supportive Care in Cancer (MASCC), and 0.868 (95% CI, 0.827 to 0.903) for CISNE (P=.002 for comparison between CISNE and MASCC).

Conclusion: CISNE is a valid model for accurately classifying patients with cancer with seemingly stable FN episodes.

Reviewer's opinion: Febrile neutropaenia remains an important complication of cytotoxic chemotherapy in patients with solid malignancies although the recent focus has been identification of the low-risk subset of patients who can be safely managed as outpatients with oral antibiotics. The MASCC (Multinational Association for Supportive Care in Cancer) score is a commonly used tool for this purpose, although it included patients with leukaemias and solid malignancies and has not been specifically validated in patients with solid tumours. The CISNE scores obtained in this study include some clinical parameters that are not part of the MASCC or Talcott model, such as stress-induced hyperglycaemia, low peripheral blood monocyte count and severe oral mucositis. The definition of febrile neutropenia in this study was conventional – temperature >38°C and absolute neutrophil count <0.5 or between 1 and 0.5 and expected to fall. The study population was clinically stable patients, with solid tumours receiving mild-moderate intensity chemotherapy, defined by the absence of renal, respiratory and cardiac failure or decompensation of chronic organ dysfunction, absence of hypotension or known severe infections in the first three hours after diagnosis. Patients with three or more risk factors on the CISNE scale had an approximately one in three chance of developing serious complications and a mortality rate of 3%. The negative predictive value of a CISNE score <3 for severe complications was almost 96%. This study validates the CISNE score as a useful measure of the likelihood of serious complications in stable febrile neutropaenic patients with solid tumours. The use of the CISNE scale may allow rational selection of patients for early discharge. – AR

Complete regression of metastatic cervical cancer after treatment with human papillomavirus-targeted tumour-infiltrating T-cells

Sanja Stevanovi , Lindsey M Draper, Michelle M Langhan, et al. Journal of Clinical Oncology 2015;10 May;33:1543-50.

Purpose: Metastatic cervical cancer is a prototypical chemotherapy-refractory epithelial malignancy for which better treatments are needed. Adoptive T-cell therapy (ACT) is emerging as a promising cancer treatment, but its study in epithelial malignancies has been limited. This study was conducted to determine if ACT could mediate regression of metastatic cervical cancer.

Patients and Methods: Patients enrolled onto this protocol were diagnosed with metastatic cervical cancer and had previously received platinum-based chemotherapy or chemoradiotherapy. Patients were treated with a single infusion of tumour-infiltrating T cells selected when possible for human papillomavirus (HPV) E6 and E7 reactivity (HPV-TILs). Cell infusion was preceded by lymphocyte-depleting chemotherapy and was followed by administration of aldesleukin.

Results: Three of nine patients experienced objective tumour responses (two complete responses and one partial response). The two complete responses were ongoing 22 and 15 months after treatment. One partial response lasted three months. The HPV reactivity of T cells in the infusion product (as measured by interferon gamma production, enzyme-linked immunospot and CD137 upregulation assays) correlated positively with clinical response (P=0.0238 for all three assays). The frequency of HPV-reactive T cells in peripheral blood one month after treatment was also positively associated with clinical response (P=0.0238).

Conclusion: Durable, complete regression of metastatic cervical cancer can occur after a single infusion of HPV-TILs. Exploratory studies suggest a correlation between HPV reactivity of the infusion product and clinical response. Continued investigation of this therapy is warranted.

Reviewer's opinion: Although Human Papilloma Virus (HPV) vaccination programs can reduce the incidence of cervical cancers in the coming decades, metastatic cervical cancer continues

to be a relatively treatment-refractory disease with a guarded prognosis. Platinum-based chemotherapy can lead to clinical responses that are relatively short-lived in most cases, although survival benefit has been demonstrated recently with the addition of the anti-angiogenic monoclonal antibody, bevacizumab, to cisplatin and paclitaxel. Thus far, despite a significant body of scientific understanding of the function of critical HPV oncogenic proteins (E6 and E7), attempts at therapeutic vaccination against these proteins have met with very limited success. This has been attributed to tumour-driven immunosuppression and generation of low-frequency and low-avidity T-lymphocyte responses. This study reports on the therapeutic effect of adoptive T-cell therapy (ACT) with HPV-specific T-cell clones in chemotherapy-refractory advanced cervical cancers, and also on immune correlates of benefit. The ACT protocol in this study included lympho-depleting chemotherapy with fludarabine and cyclophosphamide prior to cell infusion (to allow room for 'homeostatic' expansion of infused cells), and also intravenous interleukin-2 to support persistence and expansion of transferred T-cells. T-cells were selected for high purity, high CD8:CD4 ratio and reactivity against E6/E7 proteins. Patients received 30-150 x 109 T-cells prepared from biopsies of metastatic lesions. Histology included adenocarcinomas, squamous carcinoma and adeno-squamous cancers. The critical finding was that two of nine women achieved durable complete responses to therapy (ongoing at 22 and 15 months). This is in keeping with studies of ACT in patients with advanced melanoma and renal cell carcinoma. Of note, one of the complete responders had disease that was primarily refractory to chemo-radiotherapy. Toxicity related mainly to chemotherapy and IL-2, but no patients required invasive ventilatory support or renal-replacement therapy, and there were no treatment related deaths. The three responding patients received T-cell cultures with the highest frequencies of E6/E7 reactive T-cells and two patients whose cultures contained no E6/E7 reactive T-cells did not respond. An increase in frequency of T-cells producing IFN-γ in response to E6/E7 at 30 days in peripheral blood correlated with clinical benefit. The two complete responders also exhibited polyfunctional virus-specific T-cell responses (i.e. secreting cytokines in addition to IFN-γ) at day 30. E6/E7 specific T-cells were detected in peripheral blood as late as 13 months in responding patients. It will be interesting to see if this approach can be applied to other advanced HPV-driven squamous cancers (e.g. penis, oral cavity). Efforts to boost T-cell entry into metastatic deposits and persistence may improve the response rate. – AR

Nivolumab for metastatic renal cell carcinoma: results of a randomised Phase II Trial

Robert J Motzer, Brian I Rini, David F McDermott, et al.
Journal of Clinical Oncology 2015;1 May;33:1430-7.

Purpose: Nivolumab is a fully human immunoglobulin G4 programmed death–1 immune checkpoint inhibitor antibody that restores T-cell immune activity. This phase II trial assessed the antitumour activity, dose-response relationship and safety of nivolumab in patients with metastatic renal cell carcinoma (mRCC).

Patients and Methods: Patients with clear-cell mRCC previously treated with agents targeting the vascular endothelial growth factor pathway were randomly assigned (blinded ratio of 1:1:1) to nivolumab 0.3, 2, or 10mg/kg intravenously once every three weeks. The primary objective was to evaluate the dose-response relationship as measured by progression-free survival (PFS). Secondary end-points included objective response rate (ORR), overall survival (OS) and safety.

Results: A total of 168 patients were randomly assigned to the nivolumab 0.3 (n=60), 2 (n=54), and 10mg/kg (n=54) cohorts. One hundred eighteen patients (70%) had received more than one prior systemic regimen. Median PFS was 2.7, 4.0, and 4.2 months, respectively (P=0.9). Respective ORRs were 20, 22, and 20%. Median OS was 18.2 months (80% CI, 16.2 to 24.0 months), 25.5 months (80% CI, 19.8 to 28.8 months), and 24.7 months (80% CI, 15.3 to 26.0 months), respectively. The most common treatment-related adverse event (AE) was fatigue (24, 22, and 35%, respectively). Nineteen patients (11%) experienced grade 3 to 4 treatment-related AEs.

Conclusion: Nivolumab demonstrated antitumour activity with a manageable safety profile across the three doses studied in mRCC. No dose-response relationship was detected as measured by PFS. These efficacy and safety results in mRCC support study in the phase III setting.

Reviewer's opinion: For at least a decade, the systemic treatment of advanced renal cell carcinomas (clear-cell subtype) has been focused on small-molecule tyrosine kinase inhibitors with predominantly anti-angiogenic targets (VEGF, PDGF), such as sunitinib, sorafenib, pazopanib and axitinib. Inhibition of the mTOR pathway using temsirolimus or everolimus has also emerged as a valid treatment option. These recent developments led to a shift in emphasis away from immunotherapy (alfa-interferon, interleukin-2 and adoptive T-cell therapy) as a treatment modality, despite long-term recognition of renal cell carcinoma as one of the most immunogenic of human tumours, alongside malignant melanoma. This important study brings immunotherapy back into the foreground in advanced kidney cancers. Nivolumab is one of an expanding group of immune-checkpoint inhibitors targeted against the programmed-death 1/2 and PD1/2 ligand interaction. The drug is a fully humanised IgG4 antibody that interferes with PD1/2 ligand binding to PD-1. This boosts anti-tumour immune responses (in a non-antigen specific fashion) by improving T-cell priming by dendritic cells and by enhancing killing of tumour cells by primed effector T-cells. The study population included patients in the MSKCC poor risk group, those with impaired performance status, those with hepatic metastases and one-third of patients had received three or more systemic therapies for advanced disease. Almost all patients were nephrectomised. Median progression-free survival approached seven months with nivolumab at 10mg/kg and the response rate was 20%, with a median duration of response of almost two years. Median overall survival was two years. Treatment was safe with only 11% of patients developing Grade 3 or 4 adverse events. Although many adverse events required systemic corticosteroids, discontinuation of treatment due to toxicity was rare (<10%). Tumour tissue expression of PD-L1 assessed by immuno-histochemistry was a potential biomarker of benefit with a response rate of 31 versus 18% and median overall survival of not reached versus 18.2 months in tumours with greater than 5% versus <5% tumour cells PD-L1 positive. In contrast, there is no similar biomarker for the CTLA-4 antibody ipilimumab. The discrepancy between progression-free and overall survival may relate to pseudo-progression due to T-cell

infiltration of metastatic lesions and the time required to achieve T-cell activation (during which tumours may progress). Phase III trials of nivolumab are already underway in advanced RCC and their results are eagerly awaited. – AR

New England Journal of Medicine

Nivolumab and Ipilimumab versus Ipilimumab in Untreated Melanoma

Postow MA, Chesney J, Pavlick AC, et al.
N Engl J Med 2015; 372:2006-2017.
May 21, 2015DOI: 10.1056/NEJMoa1414428.

Background: In a phase 1 dose-escalation study, combined inhibition of T-cell checkpoint pathways by nivolumab and ipilimumab was associated with a high rate of objective response, including complete responses, among patients with advanced melanoma.

Methods: In this double-blind study involving 142 patients with metastatic melanoma who had not previously received treatment, we randomly assigned patients in a 2:1 ratio to receive ipilimumab (3mg per kilogram body weight) combined with either nivolumab (1mg per kilogram) or placebo once every three weeks for four doses, followed by nivolumab (3mg per kilogram) or placebo every two weeks until the occurrence of disease progression or unacceptable toxic effects. The primary end-point was the rate of investigator-assessed, confirmed objective response among patients with BRAF V600 wild-type tumours.

RESULTS: Among patients with BRAF wild-type tumours, the rate of confirmed objective response was 61% (44 of 72 patients) in the group that received both ipilimumab and nivolumab (combination group) versus 11% (4 of 37 patients) in the group that received ipilimumab and placebo (ipilimumab-monotherapy group) ($P<0.001$), with complete responses reported in 16 patients (22%) in the combination group and no patients in the ipilimumab-monotherapy group. The median duration of response was not reached in either group. The median progression-free survival was not reached with the combination therapy and was 4.4 months with ipilimumab monotherapy (hazard ratio associated with combination therapy as compared with ipilimumab monotherapy for disease progression or death, 0.40; 95% confidence interval, 0.23 to 0.68; $P<0.001$). Similar results for response rate and progression-free survival were observed in 33 patients with BRAF mutation–positive tumours. Drug-related adverse events of grade 3 or 4 were reported in 54% of the patients who received the combination therapy compared with 24% of patients who received ipilimumab monotherapy. Select adverse events with potential immunologic causes were consistent with those in a phase 1 study, and most of these events resolved with immune-modulating medication.

Conclusion: The objective-response rate and the progression-free survival among patients with advanced melanoma who had not previously received treatment were significantly greater with nivolumab combined with ipilimumab than with ipilimumab monotherapy. Combination therapy had an acceptable safety profile.

Reviewer's opinion: This is an unprecedented time in the understanding and clinical development for individuals with malignant melanoma, a heterogeneous disease with invariably poor outcome. Over the last decade, our understanding has improved considerably, thanks to genomic profiling and ongoing research. Results from several phase III trials showed considerable improvements in not only the response but in the overall survival rates using therapeutic agents with diverse mechanisms of actions. Recent approval of BRAF inhibitors for the management of locally advanced/metastatic tumours harbouring BRAF mutation has completely changed the clinical practice and improved the management outcome.

Immunotherapy is the other area of cancer research and drug development. Cutting-edge knowledge on the subject has led to the development of a large number of therapeutic agents with promising activity. In particular, so called T-cell checkpoint inhibitors are the new kids on the block. Trial results using agents like nivolumab, Pembrolizumab and azetolizumab (MPDL3280A) offer tantalising hints of possibly greater efficacy. These immunotherapeutic agents are not only establishing their place in the management of cancers such as BRAF positive malignant melanoma, but for BRAF negative tumours for which until recently the management options have been limited. Objective response rate in nearly two-third of BRAF wild-type melanoma with one in five showing complete response reported above looks like a dream come true for immunotherapy. It is comforting to know that despite combination of two relatively new therapeutic agents in this phase 1 trial, no adverse events of concern were detected. However, immune-related adverse events (irAEs) are common with T-cell checkpoint inhibitors. Although these inflammatory side effects can affect many organs, they typically involve the skin, gastrointestinal, hepatic and endocrine systems. Short-term use of immunosuppressive therapy can control these side effects without any negative impact on a favourable antitumour response. But complete understanding of the principles of irAEs development, their recognition and successful management is essential as the use of these agents increases in clinically. – SU

To have your event listed in the Oncology News diary, E: patricia@oncologynews.biz by December 4th 2015.

2015

November

BASO~ACS Scientific Conference and RSM Section of Surgery Conference 2015
1-3 November 2015; London, UK
E: rattandeepjhita@baso.org.uk or surgery@rsm.ac.uk
W: www.baso.org.uk

NCRI Cancer Conference
1-4 November 2015; Liverpool, UK
W: www.ncri.org.uk

Gynaecological Cancers - From Diagnosis To Palliative Care
4 November 2015; Preston, UK
E: education@stcatherineshospice.co.uk

The Royal Marsden Gynaecological Cancer Study Day
4 November 2015; London, UK
E: conferenceteam@rmh.nhs.uk
T: +44 (0)20 7808 2921
W: www.royalmarsden.nhs.uk/studydays

Leukaemia CARE Haematology Nurses Conference
4 November 2015; Manchester, UK
E: care@leukaemiacare.org.uk
W: www.leukaemiacare.org.uk/nurses-conferences/nurses-conference-manchester

Inaugural Guildford Supportive Care in Cancer Course
4–5 November 2015; London, UK
T: +44 (0)1483 571122 x2043
E: victoriarobinson@nhs.net
W: www.royalsurrey.nhs.uk

Breast Cancer Care Annual Conference
6 November 2015; London, UK
W: www.breastcancercare.org.uk/annual-conference

The Eighth Royal Marsden Pain and Opioid Conference
6 November 2015; London, UK
E: conferenceteam@rmh.nhs.uk
T: +44 (0)20 7808 2921
W: www.royalmarsden.nhs.uk/conferences

ESMO Summit Americas 2015
6-8 November 2015,
Miami, Florida, USA
W: esmo.org

NEW
Introduction to Cancer
9-10 November 2015; Manchester, UK
E: education.events@christie.nhs.uk
W: www.christie.nhs.uk/school-of-oncology/education-and-training.aspx

NEW
Biological Basis of Cancer: Pharmacology, Chemotherapy and Biology
9-13 November 2015; Manchester, UK
E: education.events@christie.nhs.uk
W: www.christie.nhs.uk/school-of-oncology/education-and-training.aspx

NEW
Quality of Life Head & Neck Cancer Workshop
10–11 November 2016; Liverpool, UK
W: www.headandneckcancer.co.uk

The Seventh Annual Royal Marsden Head and Neck Conference: Skin Cancer of the Head and Neck
13 November 2015; London, UK
E: conferenceteam@rmh.nhs.uk
T: +44 (0)20 7808 2921
W: www.royalmarsden.nhs.uk/conferences

NEW
UKONS 2015 Conference
13-14 November 2015; Birmingham, UK
W: www.ukons.org/conference

NEW
An Introduction to Protons in Radiotherapy
17 November 2015; Manchester, UK
E: education.events@christie.nhs.uk
W: www.christie.nhs.uk/school-of-oncology/education-and-training.aspx

African Organisation for Research and Training in Cancer's 10th International Conference on Cancer in Africa (AORTIC 2015)
18–22 November 2015;
Marrakech, Morocco
W: www.aorticconference.org
E: info@aorticconference.org

NEW
Palliative Care
19 November 2015; Manchester, UK
E: education.events@christie.nhs.uk
W: www.christie.nhs.uk/school-of-oncology/education-and-training.aspx

NEW
Lymphoma Association Clinical Nurse Specialist Masterclass
20 November 2015; Leeds, UK
W: www.lymphomas.org.uk/health-professionals
E: healthprofessionals@lymphomas.org.uk

4th Royal Marsden Lung Cancer Symposium
20 November 2015; London, UK
E: conferenceteam@rmh.nhs.uk
T: +44 (0)20 7808 2921
W: www.royalmarsden.nhs.uk/conferences

Managing Issues in Haematological Disorders in Adults
23 November 2015; London, UK
E: conferenceteam@rmh.nhs.uk
T: +44 (0)20 7808 2921
W: www.royalmarsden.nhs.uk/studydays

NEW
Haematology Nursing: Stem Cell Transplantation
23 November 2015; Manchester, UK
E: education.events@christie.nhs.uk
W: www.christie.nhs.uk/school-of-oncology/education-and-training.aspx

NEW
An Introduction to Radiotherapy
23 November 2015; Manchester, UK
E: education.events@christie.nhs.uk
W: www.christie.nhs.uk/school-of-oncology/education-and-training.aspx

NEW
Commissioning Chemotherapy Services Conference
30 November 2015; London, UK
Kirsten Wicke
T: +44 (0)1628 897 915
E: kirsten@succinctcomms.com

December

NEW
Molecular Mechanisms of Targeted Cancer Treatment
1 December 2015; London, UK
E: conferenceteam@rmh.nhs.uk
T: +44 (0)20 7808 2921
W: www.royalmarsden.nhs.uk/studydays

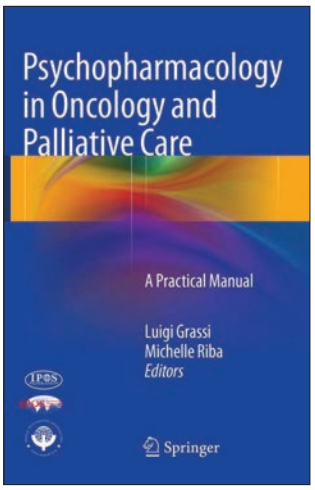
Supervisor skills workshop
3 December 2015; London, UK
W: www.rcr.ac.uk/oncologyevents
E: conf@rcr.ac.uk

NEW
The Womb Cancer Alliance Final Priority Setting Workshop
3 December 2015; Manchester, UK
Attendance by invitation only
Dr Emma Crosbie
E: emma.crosbie@manchester.ac.uk
T: +44 (0)161 701 6942

NEW
Nutrition and Survivorship: Nutritional issues following Cancer Treatment
8 December 2015; London, UK

Psychopharmacology in Oncology and Palliative Care – A practical manual

Editors: Grassi L, Riba M. Published by: Springer. ISBN 978-3-642-40133-6. Price: £72.00.



This is a multi-author book, whose intended audience is doctors working with cancer patients, including oncologists, surgical oncologists and general practitioners. The principal intent is to provide them with a guide to the recognition and pharmacological management of psychiatric disorders in oncology patients.

The book is generally readable although the text is dense and there is occasionally some idiosyncratic language and sentence construction. Each chapter is individually and extensively referenced and there are many useful summary tables and boxes. The index has been well compiled.

The book is divided into three parts. The first comprises seven chapters and addresses general aspects of the use of drugs in psychiatric and related problems arising in oncology. Chapter 1 is a general overview while Chapter 2 looks at pharmacokinetics and pharmacodynamics. In Chapters 3 and 4, the focus is on assessment and diagnosis. Chapter 5 discusses the importance of communication and some of the aids to enhance clinician-patient interaction. In Chapter 6 the authors explain the way patients react individually to cancer-related events and they attempt to help the clinician to assess whether medication or some other intervention such as psychotherapy is most appropriate. Chapter 7 explores some complementary therapies and their integration into cancer care, particularly as an alternative to pharmacological intervention.

The middle section of the book contains nine chapters, most of which look at the recognition and medical management of specific psychiatric and psychological conditions. In Chapters 8 and 9 the authors discuss anxiety, depression and stress-related disorders. The use of psychotropic drug treatment of somatoform disorders, such as pain, fatigue and anorexia, experienced by cancer patients is covered in Chapter 10. Chapter 11 is about bipolar disorder and major depressive disorder while Chapter 12 explores the treatment of delirium. Chapters 13 and 14 are about the management of psychotic conditions and sleep disorders. Chapter 15 covers substance abuse, including prescription medicines and alcohol, in oncology.

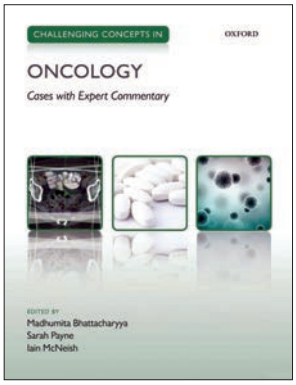
The final part of the book comprises six chapters and the first three of these (Chapters 17 – 19) deal with psychiatric emergencies in cancer patients and psychopharmacology in both younger patients and in the elderly. Chapter 20 looks at sedation for psychological distress at the end of life, Chapter 21 at research in psychopharmacology and finally Chapter 23 explores diverse ethical issues around this kind of treatment.

In summary, this book comprehensively covers the use of psychotropic drugs in the treatment of psychiatric disorders in oncology, as well as addressing their use in ameliorating some of the common side effects of cancer and its treatment. It aims to help the oncologist recognise and manage these conditions and to interact effectively with their patients. Although the price is quite high, the book would be a useful purchase for any clinician involved in the care of cancer patients.

Kathleen Mais,
Nurse Clinician Head & Neck Oncology,
The Christie, Manchester, UK.

Challenging Concepts in Oncology – Cases with Expert Commentary

Edited by Madhumita Bhattacharyya, Sarah Payne, Iain McNeish. Published by: Oxford University Press. ISBN: 978-0-19-968888-3. Price: £49.99.



This 298 page paperback book portrays 25 clinical cases of common cancers and common cancer related complications. It is written primarily for medical and clinical oncology trainees, with the MRCP3 examination and the FRCR in mind. The book is also useful for more senior doctors hoping to gain an overview of the management of other tumour sites.

All of the 24 experts and 28 contributors to the book are from the UK, reflecting current practice within Great Britain.

For each case there is a presentation or case history followed by treatment or discussion. Throughout the text are interspersed many blue boxes such as learning points, clinical tips, expert comments and evidence base. The diagnostic and investigative features of particular cancers are displayed in the learning point boxes. The evidence base boxes displays the relevant clinical trial data using an easy to read bullet-point format. Dark blue boxes contain the "expert comment" and are placed throughout the chapter; however I found the text against a dark background difficult to read. The conclusion of the chapter is presented as a "final word from the expert" and summarises the current situation for that tumour site. Each chapter is reviewed by a national/ international expert. All of the chapters are well referenced.

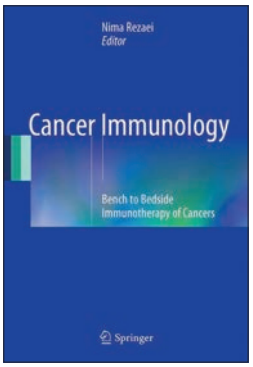
The range of topics discussed was large and, broadly representative of every day clinical practice. I found the clinical scenarios to be interesting and thought provoking.

Overall I found the book pleasurable to read, it did not appear to be intimidating or daunting; rather the opposite. It allows the reader to test him or herself against the authors. The reader may use this book in preparation for examinations as the boxes present a lot of up-to-date information in an easy to read format, which can be used as revision aides. My only criticisms; were that the photographs were black and white, whereas colour photographs would be more helpful especially for showing pathology slides and rashes. NICE guidance of cancer treatment which often dominates and determines management plans of cancer in the UK did not feature prominently in the book and that the font size within the boxes was rather small. In summary this is a useful book especially for those preparing for examinations.

Dr Karin Baria,
Retired Consultant Clinical Oncologist.

Cancer Immunology – A Translational Medicine Context

Editor: Nima Rezaei. Published by: Springer. ISBN: 978-3-662-44005-6. Cost: ebook £136.50. Hardcover: £171.00.



This hardback text of 597 pages is the second of a three volume series on cancer immunology. This book focuses on the immunopathology of cancers. There are 85 world-wide contributors to this book, the forward being written by Francesco Marincola. This book is written for those researchers and clinicians who want to move the field forward at a clinical and scientific level. I found this book to be a highly specialist text on cancer immunology. There are 26 chapters most of which are concerned with the detailed, scientific aspects of cancer immunology. The initial chapters are concerned with the scientific aspects of cancer immunology; e.g. apoptosis and cancer, role of cytokines in tumour immunity the latter deal with more clinical matters. For instance Chapter 18: Primary immunodeficiencies and cancer discusses the interplay between primary immunodeficiencies; e.g. X-linked Agammaglobulinaemia and the formation of malignancy. As the life expectancy of such patients increases so does the risk of developing cancer, partly due to involvement of chronic antigen stimulation, oncogenic viruses, and impaired immunity. The changes seen in the innate and adaptive immune systems with advancing age are explored as a mechanism for developing cancer, in chapter 19: Immunosenescence, Oxidative Stress and Cancers. Low grade inflammation seen with aging is postulated as a common factor linking diseases of old age and genomic instability, metabolism and immunity are interlinked in the formation of cancer and other inflammatory related diseases.

Chapter 20: Nutrition, Immunity and Cancers, provides an explanation of how the imbalance of cytokine production and neuropeptide and adipokine dysfunction has major consequences for the nutritional aspects of the cancer patient. It also discusses the dietary causation of cancer (obesity) and the role of minerals, vitamin intake and the immune status.

Chapter 26: Immunohistochemistry of cancers. I found this to be a comprehensive and clinically relevant chapter on the use of immunohistochemistry (IHC) in diagnostic pathology; helping to provide evidence of cellular lineage and sub-typing of lesions and malignancies. This chapter provides the reader with examples of colour photographs of IHC of all tissue types and shows how prognostic and therapeutic applications have become the norm, enabling targeted therapies to be used in treatment of tumours. This chapter is really useful for the clinician and has direct clinical applications.

In summary this is a specialist text on cancer immunology, it is well written, illustrated with lots of colour photographs, diagrams and tables, and the chapters are very well referenced. I feel that this book is an asset to researchers and clinicians.

Dr Karin Baria,
Retired Consultant Clinical Oncologist.

BTOG 2016

14th Annual BTOG Conference 2016

Wednesday 27th January to Friday 29th January – Dublin

BTOG Chair, Dr Sanjay Popat

Feedback from BTOG 2015

"I like the multidisciplinary aspect and opportunity to learn from other specialties."

"Excellent conference with a good range of speakers from all the different disciplines and audience members."

"Fantastic mix of all aspects of Thoracic Cancer management – BTOG feels like all the good bits of a massive MDT meeting with added social aspects."

"An excellent learning forum, with pertinent and up-to-date presentations which were evidence based topics and news on current studies and trials."

IMPORTANT DATES

Poster submission: Opens 1st August 2015 • Closes 1st October 2015
Registration and hotel booking opens 1st September 2015

BTOG is a multi-disciplinary group for professionals involved with thoracic malignancies.
BTOG aims to improve the care of patients with thoracic malignancies through multidisciplinary education, developing and advising on guidelines for patient care and facilitating and nurturing clinical trial ideas into full protocols.
BTOG Chair: Dr Sanjay Popat

BTOG Secretariat

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Latest developments on products and services from the industry. To have your news included contact Patricia McDonnell at Oncology News on T/F: +44 (0)288 289 7023, E: patricia@oncologynews.biz

episil® liquid – a barrier to oral mucositis pain

episil® oral liquid is an innovative treatment for intraoral pain associated with oral mucositis. Oral mucositis, a painful side effect of cancer treatments, has a large pharmacoeconomic impact and affects cancer patients' quality of life.

episil® oral liquid has been clinically proven to provide rapid, effective, and long-lasting pain relief by creating a bioadhesive, barrier-forming lipid membrane that coats the oral cavity. Without producing a numbing effect, the product soothes inflammation and painful ulcerations, thereby helping patients to maintain their quality of life while undergoing cancer treatment.

With episil® liquid there is no need for mixing or measuring of medications before use as it comes in a ready-to-use, pocket-sized, pump device, and can conveniently be applied right before meals.

The product doesn't cause systemic side effects and won't interfere with other medications.

episil® oral liquid is a registered medical device, Class I, listed on Drug Tariff, and can be prescribed on an FP10.

episil® liquid – effective relief of oral mucositis pain, within five minutes and for up to eight hours.

For further information visit: www.camurus.com

Provectus Biopharmaceuticals completes patient accrual for PH-10 Phase 2 Clinical Study of cellular and immunologic changes in the skin

Provectus Biopharmaceuticals, Inc. announced recently that it has completed patient accrual for its phase 2 study of the cellular and immunologic changes in the skin of patients receiving PH-10, an investigational topical treatment for atopic dermatitis and psoriasis.

This phase 2 trial is a multicenter study of subjects with mild to moderate psoriasis. Subjects apply PH-10 vehicle daily for 28 consecutive days followed by active PH-10 daily for 28 consecutive days to their plaque psoriasis areas on the trunk or extremities (excluding palms, soles, scalp, facial and intertriginous sites). Biopsies of one target plaque are collected at baseline (at least seven days prior to first study treatment on day one) and at days 29 and 64, with a seven-day interval between biopsy at day 29 and commencement of application of active PH-10 on day 36. Study data from each subject will serve as an internal control (i.e., assessment at baseline and at the end of application of PH-10 vehicle) for assessment of clinical and cellular response to active investigational agent.

Further information is available at https://clinicaltrials.gov/ct2/show/record/NCT02322086.

PROVECTUS BIOPHARMACEUTICALS, INC.

Varian Medical Systems publishes 2015 Sustainability Report

Varian Medical Systems have announced the publication of its annual corporate social responsibility report, detailing the company's policies and achievements in extending access to cancer care, protecting resources, and helping to save lives.

The Varian 2015 Sustainability Report has been produced as part of a wider company effort to continually improve sustainability performance and transparency. As a result, Varian is increasingly recognised as a leader in the field and was rated among the greenest companies in the U.S. by the Newsweek Green Rankings for 2014. In January 2015, Varian was the highest ranked medical device company in the Corporate Knights Global 100 listing of the most sustainable corporations in the world.

"It comes naturally to Varian to want to contribute not only to saving lives by providing affordable access to advanced cancer care but to improving lives through good corporate citizenship," said Dow Wilson, chief executive officer of Varian Medical Systems. "We strive to maximise the positive effects of our activity by weaving sustainability into every aspect of business, meeting climate change and other environmental challenges, delivering safe and effective products, and measuring our social impact in meaningful ways."

Varian's 2015 Sustainability Report is available to download at: www.varian.com/about-varian/citizenship

Chasing zero hair loss during chemotherapy

UK based Paxman – pioneers in scalp cooling – recently unveiled their commitment to 'chase zero hair loss during chemotherapy' at the 2015 European Cancer Congress, in Vienna, Austria.

A global leader in scalp cooling, Paxman continues to heavily invest in new R&D, funding multi-disciplinary research groups and conducting clinical trials to help improve the efficiency of scalp cooling and ultimately raise the success rate of 'zero hair loss' from 50/50 to 80/20 by the year 2020.

As part of this commitment, Paxman have founded an international multi-disciplinary special interest group (SIG) to look into chemotherapy-induced alopecia (CIA) and scalp cooling. Research will include reduced post infusion cooling times, further in-vitro modelling to better understand the mechanisms of scalp cooling, understanding the role in temperature with different chemotherapy regimens and measuring patient comfort.

As well as this patient focussed research,

Paxman is also undertaking a series of clinical trials in the UK, the US, Japan, Australia, Germany and Austria and is also developing a third-generation of the cooling cap to ensure it fits people's heads more efficiently.

Richard Paxman Managing Director of Paxman, said: "We know scalp cooling works so our aim is to raise the success rate for all patients undergoing chemotherapy so no one ever has to lose their hair as a side effect of cancer."

For more information visit www.paxmanscalpcooling.com

ONCOblot® expands international distribution

Cancer confirmation test now available in united kingdom

Developed by Mor-NuCo in West Lafayette, Indiana, the ONCOblot® Test detects a specific protein shed into the circulation from malignant cancer cells only. For the first time since its inception, ONCOblot® is now available in the United Kingdom through distribution by RCLIN, Geneva, Switzerland.

"Our test being available in the UK means we are one step closer to the very inherent goal of this test," says Nick Miner, VP of Business Development for, Mor-NuCo, LLC, "to change the way we address and fight cancer around the world," he continued.

The test works by detecting ENOX2 proteins unique to malignant cancer. ONCOblot® can reveal 26 primary cancers from 20 different organ sites as early as Stage 0.

The ONCOblot® Test is a key component to treating cancer because it gives patients and physicians the insights for successful cancer management. Never before has one test been able to detect cancer on such a microscopic level and provide so much knowledge for early intervention and on-going management.

If you'd like more information about the ONCOblot® Test, please visit www.oncoblotlabs.com or E: info@oncoblotlabs.com

ONCOblot®
Cancer Testing with Confidence
The answer is in the blot.

Provectus Biopharmaceuticals announces initiation of Phase 1b/2 Clinical Trial to study PV-10 in combination with iImmune check point inhibitor pembrolizumab

Provectus Biopharmaceuticals, Inc. announced recently that it has completed development of the protocol for Phase1b/2 testing of its investigational cancer drug PV-10 in combination with pembrolizumab in patients with Stage IV melanoma. Pembrolizumab (also known as Keytruda®, a product of Merck and Co. Inc.) is an immune checkpoint inhibitor approved for treatment of patients with advanced or unresectable melanoma. PV-10 is Provectus's novel investigational drug for cancer that is injected into solid tumours (intralesional administration); it is currently undergoing Phase 3 clinical testing in patients with Stage III melanoma. Clinical testing under the new Phase 1b/2 protocol is expected to commence before the end of the year.

The combination protocol enables initial clinical testing of concepts at the center of a patent held by Provectus, U.S. Patent number 9,107,887, which Pfizer, Inc. (PFE) jointly owns. Specifically, the patent covers the use of PV-10 in combination with systemic inhibitors of immune system down-regulation, such as anti-CTLA-4, PD-1 and PD-L1 immune checkpoint inhibiting antibodies. Pembrolizumab is an anti-PD-1 antibody. Pre-clinical testing of PV-10 used in combination with these important classes of drugs demonstrated potential importance for treatment of advanced cancers.

The FDA granted accelerated approval to pembrolizumab in September 2014, making it the first FDA-approved anti-PD-1 immune checkpoint inhibitor. Because pembrolizumab is already FDA-approved, Provectus can commence this study with or without assistance of a partner.

For further details on the protocol visit https://www.clinicaltrials.gov/ct2/show/NCT02557321

PROVECTUS
BIOPHARMACEUTICALS, INC.

Oncotype DX® test predicts chemotherapy benefit in early-stage breast cancer

Genomic Health have announced the presentation of the first results from the Trial Assigning IndividuaLised Options for Treatment (Rx), or TAILORx, a large, prospectively conducted trial. Presented at the 2015 European Cancer Congress (ECC2015), results from a group of 1,626 patients with a Recurrence Score result between 0 and 10 demonstrated that 99.3 percent of patients with node-negative, oestrogen receptor-positive, HER2-negative breast cancer who met accepted guidelines for recommending chemotherapy in addition to hormone therapy had no distant recurrence at five years after treatment with hormone therapy alone. Outcomes were excellent irrespective of patient age, tumour size, and tumour grade.

'The Oncotype DX test allows for a better understanding of individual tumour biology and gives greater confidence in recommending a treatment plan best suited for an individual patient.' said Nigel Bundred, Professor in Surgical Oncology, University Hospital of South Manchester NHS Foundation Trust

For more information, please visit, www.GenomicHealth.co.uk or www.OncotypeDX.com

Provectus Biopharmaceuticals reports publication of review paper on PV-10 tumour ablation and immune stimulation

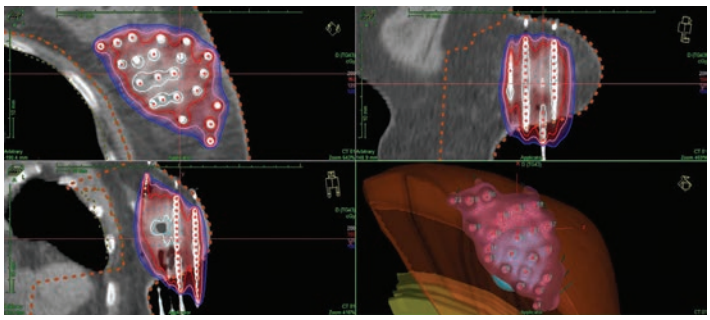
Provectus Biopharmaceuticals, Inc. reported that the Journal of Clinical and Cellular Immunology has published a paper titled, "The Potential of Intralesional Rose Bengal to Stimulate T-Cell Mediated Anti-Tumour Responses." The paper can be found online at http://www.omicsonline.org/open-access/the-potential-of-intralesional-rose-bengal-to-stimulate-tcell-mediated-antitumour-responses-2155-9899-1000343.php?aid=59072

Authors Ajay V Maker, Bellur Prabhakar, and Krunal Pardiwala state that their "article serves to evaluate the potential of intralesional rose bengal [RB] to stimulate T-cell mediated anti-tumour responses in in-vitro, pre-clinical, and clinical studies." The review covers findings in both animal models and human clinical trials covering the use of intralesional RB in the treatment of: melanoma, breast cancer, ovarian cancer, gastric cancer and sarcoma.

They conclude, "Our current research is establishing the role of RB in generating anti-tumour immune responses in gastrointestinal cancer and liver metastases. Decrease in tumour burden and stimulation of an immune response with PV-10 has been demonstrated in animal models of metastasis, and correlations of these responses in clinical studies is consistent with such results. That PV-10 treatment can potentially increase circulating cytotoxic T-cells, even in patients who were previously treated with immune-activating checkpoint blockade, supports the possibility that RB induced cytotoxicity may activate T-cells that are responsible for the bystander effect on untreated lesions. As such, intralesional therapy with RB may be a promising new mode of therapy to stimulate T-cell mediated anti-tumour immune responses."

For further information visit: www.pvct.com

APBI breast cancer treatment shortens therapy time from weeks to days



New data demonstrate that accelerated partial breast irradiation (APBI) with brachytherapy is clinically equivalent to whole breast irradiation in treating early stage breast cancer.

The Groupe Européen de Curiethérapie of the European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) revealed results from a randomised controlled, multicenter, phase III study comparing APBI with interstitial multi-catheter brachytherapy to whole breast irradiation (WBI).

Ben Pais, Vice President Medical Affairs at Elekta says: "APBI with brachytherapy has several potential benefits in the treatment of patients with early stage breast cancer. It can reduce the course of radiation therapy from between five to seven weeks down to only four or five days. And since it is delivered to a specific region of the breast, it reduces the total radiation exposure by four-fold to healthy surrounding tissue and nearby structures including the chest wall, heart, lungs or skin."

"The GEC-ESTRO study is the most comprehensive clinical study to date evaluating the efficacy of multi-catheter APBI brachytherapy alone versus traditional external whole breast irradiation," said Prof. Vratislav Strnad, chair of the GEC-ESTRO Breast Cancer Working Group.

For further information email: andre.silveira@elekta.com

Varian Stages RapidArc SRS Seminar at Clatterbridge

Radiotherapy professionals from eight leading UK cancer centres attended a seminar recently to learn more about the use of Varian's RapidArc system for stereotactic treatments of multiple metastases.

The 60 attendees came from hospitals that either already deliver stereotactic radiosurgery (SRS) or stereotactic body radiotherapy (SBRT) treatments or who are about to commence such treatments via the NHS England commissioning process. They travelled to Clatterbridge Centre for Oncology in the Wirral to hear from global SRS experts.

Doctors from leading centers in the UK, Amsterdam and Milan spoke about their experiences delivering advanced stereotactic treatments with RapidArc for multiple metastases in the brain and spinal cord.

"Only 13 sites in the UK have been allocated permission to deliver SRS treatments and well over half of these were represented at this seminar," said Adele Lyons, regional sales manager with Varian Medical Systems.

Leading cancer centres attending the event included those in Plymouth, Ipswich, Edinburgh, Glasgow, Guildford, Newcastle and London (University College Hospital and Guy's & St. Thomas'), as well as several attendees from the host hospital, Clatterbridge.

For further information contact:
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E: neil.madle@varian.com
W: www.varian.com

Dad who inspired unique fundraiser passes away

Steve Lloyd, with wife Angela and footballer Carl Jenkinson at the Brain Tumour Research fundraiser.

A father-of-two whose brain tumour battle inspired a unique cycling event to raise funds for research has passed away.

Steve Lloyd, 39, from Essex, was diagnosed with an aggressive glioblastoma multiforme (GBM) in 2008. His death, on 27th September, came just three days after the achievements of dozens of cyclists who pedalled the length of the District underground line were recognised at the opening of a new brain tumour research centre.

The District Line Cycle Challenge, which took place in August, raised more than £25,000 for the charity Brain Tumour Research with friends and colleagues at Transport for London cycling 74 miles along the District line. Steve was a life-long West Ham fan and the event was supported by Hammers' full-back Carl Jenkinson.

The cyclists' efforts were commemorated with a unique tile on a "Wall of Hope" at the new Centre of Excellence in partnership with Imperial College Healthcare NHS Trust. Each tile is dedicated to patients, their families, friends and corporate supporters and represents the £2,740 it costs to fund a day of research.

For further information visit: www.braintumourresearch.orgorg/work-for-us

Thousands raised in memory of Stephen McKiernan

Thousands of pounds have been raised for Macmillan Cancer Support in memory of SDLP press officer Stephen McKiernan, who died recently.

Stephen's close friend Ciaran McElholm and Frank McDonnell cycled almost 50 miles from Trillick to Derry via Dromore in his memory, raising £4,415 in the process.

SDLP Foyle MLA Pat Ramsey met the men on their arrival in Derry said: "Stephen was highly respected and loved by all the SDLP parliamentary team and all staff in parliament buildings in Stormont and Westminster.

"He was a very proud member of the SDLP staff team but a dedicated and unselfish senior press officer who took great pride in all the work he did. We will miss him badly.

"Stephen's bravery in the face of all his challenges was inspirational. It's fitting that his friends continue to inspire others in his name. Ciaran and Frank deserve huge credit for their arduous cycle and the significant fundraising effort they've made."

Frank McDonnell and Ciaran McElholm.

Mr Ramsey also paid tribute to Macmillan Cancer Support.

He said: "Macmillan Cancer Support is doing amazing work every day with those dealing with cancer and their families.

"Stephen had previously run the Belfast Marathon to raise funds to support this excellent work and I'm sure he'd be so proud of his friends for carrying on in his memory."

Ariane Medical Systems welcome news from NICE of use of Low energy contact Xray brachytherapy for early stage rectal cancer

The pioneering non-surgical treatment for early-stage rectal cancer has now been formally approved by The National Institute for Health and Care Excellence (NICE).

The low energy, high dose Papillon technique is an alternative to surgery and was introduced to the UK in 1993 at The Clatterbridge Cancer Centre by Prof Arthur Sun Myint. Since 2006 Prof Myint has treated over 600 patients using Ariane Medical systems Ltd Papillon50 treatment system; with another 11 centres around Europe.

Professor Myint, commented: "The NICE approval will be of great benefit to patients who may not be fit enough for the surgical treatment and younger patients who would otherwise need a stoma to treat their rectal cancer. It is very good to know that more patients in the UK will be able to get the benefits of the Papillon technique especially in the treatment of early diagnosed rectal cancer."

R to L - Head Radiographer CCC Kate Perkins, Prof Sun Myint, PAPS Macmillan patient support head Sue Davies, Papillon patient Mark Davies (Photo copyright (Adam Slama), courtesy of Macmillan Cancer Support).

For further information visit: www.arianemedicalsystems.com

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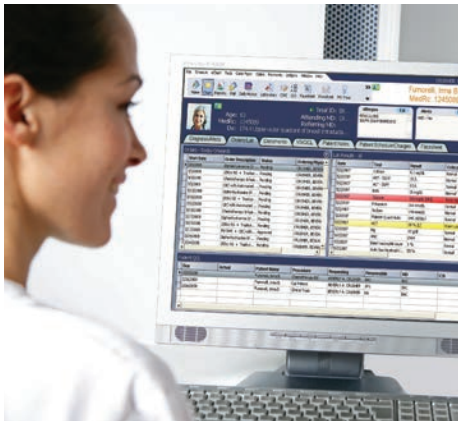

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