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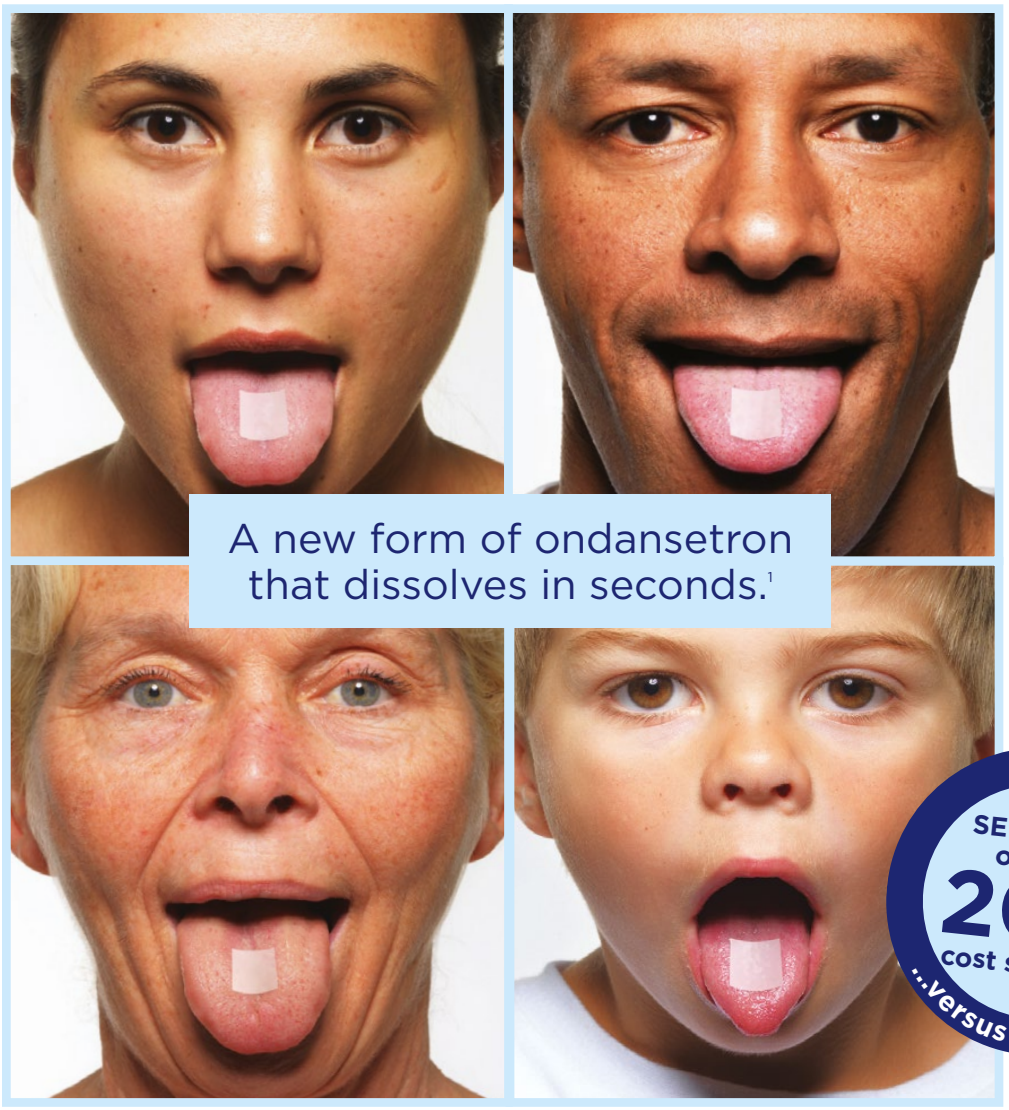

Setofilm 4mg and 8mg orodispersible films. Abbreviated Prescribing Information
REFER TO THE SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) BEFORE PRESCRIBING. **Presentation:** Orodispersible films containing 4mg or 8mg of ondansetron. **Indication:** *Adults:* Prophylaxis of acute nausea and vomiting induced by moderately emetogenic chemotherapy. Prophylaxis and treatment of delayed nausea and vomiting induced by moderately to highly emetogenic chemotherapy. Prophylaxis and treatment of acute and delayed nausea and vomiting induced by highly emetogenic chemotherapy. Prophylaxis and treatment of post-operative nausea and vomiting (PONV). *Paediatric population:* Management of chemotherapy induced nausea and vomiting (CINV) in children aged ≥6 months. Prophylaxis and treatment of PONV in children aged ≥4 years. **Dosage and administration:** Setofilm is indicated for oral use. The film should be placed on to the tongue and will disintegrate without water in a few seconds. Setofilm may be recommended in patients with an enhanced risk of aspiration and in patients that experience difficulties in swallowing. Adults and elderly: The dose of ondansetron should depend on the indication. *Emetogenic chemotherapy and radiotherapy* 8mg 1 to 2 hours before treatment, followed by 8mg 12 hours later. After 24 hours, 8mg twice daily may be continued for up to 5 days. *Highly emetogenic chemotherapy* 24mg taken with oral dexamethasone sodium phosphate 12mg, 1 to 2 hours before treatment. After 24 hours, this may be followed by 8mg twice daily for 5 days. *Prevention of PONV* 16mg one hour prior to anaesthesia or 8mg 1 hour prior to anaesthesia, followed by a further 2 doses of 8mg at 8 hourly intervals. There is limited experience on the use of ondansetron in elderly patients with PONV. In patients with moderate or severe impairment of hepatic function, the maximum daily dose should not exceed 8 mg. *Children:* The dose for treatment of CINV is calculated based on body surface area (BSA) or weight – see table 1. The dose may be continued for up to 5 days and must not exceed adult dose of 32mg.

Table 1: BSA and Weight based dosing for Chemotherapy

BSA	**Day 1[a,b]**	**Day 2-6[b]**
<0.6m²	5mg/m² i.v*plus 2mg**orally after 12 hrs	2mg** orally every 12hrs
≥0.6m²	5mg/m² i.v*plus 4mg**orally after 12 hrs	4mg orally every 12 hrs
Weight	**Day 1[a,b]**	**Day 2-6[b]**
≤10kg	Up to 3 i.v*doses of 0.15mg/kg every 4 hrs	2mg** orally every 12hrs
>10kg	Up to 3 i.v*doses of 0.15mg/kg every 4 hrs	4mg orally every 12 hrs

a The intravenous dose must not exceed 8mg.
b The total daily dose must not exceed adult dose of 32mg.
*SETOFILM is an oral preparation only, and is not available in an intravenous formulation. **SETOFILM is only available in films of 4mg and 8mg. It is not possible to divide the film to obtain a 2mg dosage. The dose for children weighing ≥40kg is 4mg Setofilm, one hour prior to anaesthesia, followed by one further dose of 4mg after 12 hours. **Contra-indications:** Hypersensitivity to ondansetron or to other selective 5-HT3-receptor antagonists or to any of the excipients. Concomitant use with apomorphine. **Warnings and precautions for use:** Use with caution to patients who have or may develop QT prolongation, patients taking other medicinal products that lead to QT prolongation, cardiac rhythm or conduction disturbances, significant electrolyte disturbances and patients treated with anti-arrhythmic agents or beta-adrenergic blocking agents. Patients with sub-acute intestinal obstruction and with adeno-tonsillar surgery should be carefully monitored following ondansetron administration. Paediatric patients with hepatotoxic chemo-therapeutic agents should be monitored closely for impaired hepatic function. It should be noted that when administering three doses at 4 hourly intervals, the total daily dose will be higher than if one single dose of 5mg/m² followed by an oral dose is given. The comparative efficacy of these two different dosing regimens has not been investigated in clinical trials. **Interactions:** Phenytoin, carbamazepine and rifampicin are potent inducers of CYP3A4 and therefore decrease ondansetron blood concentration levels. Ondansetron may reduce the analgesic effect of tramadol. Use of ondansetron with QT prolonging drugs may result in additional QT prolongation. Use with cardiotoxic drugs may increase risk of arrhythmias. **Pregnancy and lactation:** Use in pregnancy or breastfeeding is not recommended. **Side effects:** A very common side effect reported is headache. Common side effects are sensation of warmth or flushing and constipation. Other effects that have been reported are hypersensitivity reactions, including anaphylaxis, transient visual disturbances, QT prolongation, arrhythmias . For full list and frequency of adverse events, consult with the SmPC. **Licensing and Legal Category:** Legal Category: POM. Cost: Basic NHS price: £28.50 for 10 by 4mg orodispersible films. NHS price: £57.00 for 10 by 8mg orodispersible films. MA number: PL: 20142/0011 (4mg) and PL 20142/0012 (8mg). **For further information contact:** Norgine Pharmaceuticals Limited, Moorhall Road, Harefield, Middlesex, UB9 6NS. Tel: 01895 826606. E-mail: medinfo@norgine.com. SETOFILM® is a registered trademark. **Date of preparation/revision:** SE3472-MAY-2013.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Medical Information at Norgine Pharmaceuticals Ltd on 01895 826606.

References:
1. SETOFILM® Summary of Product Characteristics. Norgine, 2013.
2. MIMS, May 2013.

Date of preparation: July 2013. **SE/3650/JUL/13.**

NORGINE

Out of Africa – from skin to scrotum

Denys Wheatley, Editor.

Loss of skin pigmentation as early hominids left Africa and migrated North undoubtedly led to an increased risk of cancer. Since many cancers take decades to develop, with the majority arising and becoming life-threatening in post-reproductive years, the trade-off was good. In brief, human evolution by natural selection results in the retention of mutations that are generally beneficial, but some can incidentally have detrimental "side effects" – all life is a compromise.

The story goes that, to get the benefits in weaker sunlight of the uv radiation needed for vitamin D conversion, skin pigmentation was lost as mankind moved to temperature zones. But protection from the damaging rays of the sun was still needed. Sunburnt cells of fair skin activate p53, which, via its response elements, elicits KITLG production, stimulating melanocytes to synthesis melanin – in brief, a pathway of signalling returns the situation to square one. But genes are susceptible to mutations, many of which are lost that have no selective advantage, whereas some survive selection pressure, resulting in polymorphism. The smallest change that can occur in a gene is a (single) point mutation, where a one nucleotide has been substituted by another, and there seem to be many in p53 and its response elements.

p53 is one the pivotal proteins in controlling the fate of cells; it is a juggler than has so many response element associations with the genome that it can subtly twist cell behaviour from one direction to another, in this case from one extreme (survival and continued proliferation) to another (cell death by apoptosis). When malignant cells arise, wild-type p53 should direct them down the latter pathway. It follows that any mutation of p53 or its response elements might disturb this sensitive control over a multitude a genes, notably here the ones that induce apoptosis, particular in aberrant (potentially malignant) cells. Most of these changes that are detrimental to life are weeded out by natural selection, but the process is not fool-proof. The one in the focus of new research, KITLG p53 RE SNP, rs4590952, has slipped through quality control, and its positive selection and benefit in stimulating melanocytes is not without impunity. Using genomic analysis, Gareth Bond of the Ludwig Foundation Oxford (UK) Branch and Douglas Bell of the US National Institute of Environmental Health looked at almost 63,000 SNPs that might be related to cancer in which p53 has some operational control over transcription1. This particular variant of KITLG allows DNA damaged testicular stem cells to continue proliferating, the outcome being an increased risk of testicular cancer in white (Caucasian) men. With this recognizable marker, the development of appropriate tests indicating risk becomes a distinct possibility, as well as being indicative in prognosis of these cancers, and possibly giving some insight into treatment options.

This interesting finding follows on from Gareth Bond's work on several other polymorphisms in the last few years2,3. Clearly this is an Aladdin's if the group in Oxford can make similar associations along with other regulators of the cell cycle from the enormous number of SNPs being screened. But the story does not stop there, for this unwelcome side effect of KITLG p53 RE SNP, rs4590952 polymorphism remains to the detriment of the white men (Caucasians) because this variant is 4-5 times more common in them than Africans, which correlates with the incidence of testicular cancer, quoted as being only 25% as prevalent in Africans. So what about Inuit Indians, native American Indians, Mongols, Maoris and many other races; does skin pigmentation alone correlated here with testicular cancer? (Ironically, the one well pigmented area of the male body is the scrotum, which seldom gets sunburnt!) Some statistics can help, for the incidence of testicular cancer varies markedly worldwide (average 1.5 per 100,000 - which has doubled over the last 40 years4); but for different regions, in increasing order of magnitude (according CR UK5), the figures are: West Africa 0.2; North Africa 0.6; SE Asia 0.8; West Asia 1.5; Central Asia 3.7; Northern Europe 6.7; and Western Europe 7.8. I am in the last category; my risk of testicular cancer, while exceedingly slim, is in fact almost 40 times greater than for a West African, indicating many other mitigating factors.

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Publisher: Patricia McDonnell

Web: www.oncologynews.biz

Advertising and Editorial Manager:
Patricia McDonnell • **E:** Patricia@oncologynews.biz
T/F: +44 (0)288 289 7023 • **M:** +44 (0)7833 185116

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Meet the Editorial Team

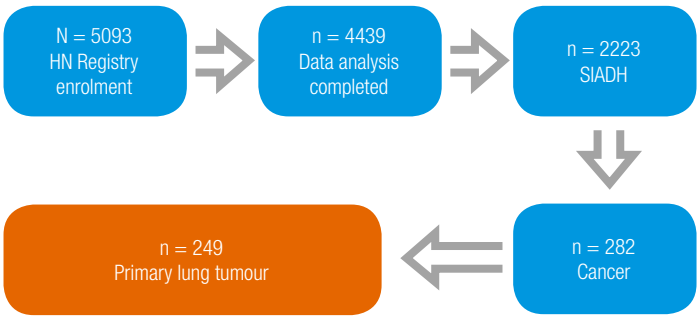
Small cell lung cancer (SCLC) and hyponatraemia: real-life data from a multicentre registry

Hyponatraemia is common in SCLC, and can have a significant impact

Hyponatraemia (low serum sodium) occurs in 11–15% of patients with SCLC.[1] It is often caused by the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), which arises from ectopic secretion of arginine vasopressin (AVP, also known as antidiuretic hormone), or by agents used in SCLC treatment and palliative care.[1] Hyponatraemia is significantly associated with shorter survival in SCLC,[1-3] and may delay or restrict the choice of chemotherapy.[1,4] In addition, hyponatraemia is known to cause symptoms which negatively affect patients' physical and mental well-being.[5]

Interim results from a prospective global registry of euvolaemic and hypervolaemic patients with hyponatraemia ([Na^+] ≤130 mEq/L) showed that 11% (249/2223) of patients with hyponatraemia attributed to SIADH had lung cancer.[6,7]

Lung cancer cohort in HN Registry



Could optimisation of hyponatraemia management help improve outcomes in SCLC?

Normalisation of serum sodium above 138 mmol/L significantly increased median survival (13.32 vs 5.16 months) in a retrospective study of 2048 patients with lung cancer.[3] There are several scenarios in which treatment for hyponatraemia secondary to SIADH in SCLC could be initiated:

- Before chemotherapy, if hyponatraemia is impacting well-being or delaying chemotherapy, or if adequate hydration is required for recommended therapy regimens[1,4]
- During and/or between chemotherapy cycles, if hyponatraemia remains uncorrected or leads to patients being readmitted
- When chemotherapy is not an option, if symptoms of hyponatraemia are affecting quality of life

Treatment options for the management of hyponatraemia secondary to SIADH

Interim results from the global hyponatraemia Registry showed that, of the commonly used interventions for hyponatraemic patients with lung cancer, hypertonic saline and vaptan therapy produced the largest rates of increase in serum sodium (with hypertonic saline producing the fastest rate of change and vaptan therapy the largest mean change).[6]

Fluid restriction was no more effective than no specific therapy for hyponatraemia.[6] Overall survival was not assessed.[6]

Treatment duration and rate of [Na^+] change in patients treated with monotherapy for HN (all monotherapy episodes)[a,6]

	Mean treatment duration ± SD (days)	Mean change in [Na^+] ± SD (mEq/L)[b]	Mean rate of [Na^+] change ± SD (mEq/L/day of treatment)
HN untreated (n = 51)	7.9 ± 7.9	3.9 ± 6.2	0.5 ± 0.8
Fluid restriction (n = 71)	4.5 ± 4.9	1.9 ± 5.3	0.4 ± 1.2
Normal (0.9%) saline (n = 64)	3.2 ± 4.0	3.0 ± 5.8	0.9 ± 1.5[c]
Hypertonic saline (n = 9)	2.2 ± 1.1	5.8 ± 4.8	3.0 ± 2.5
Vaptan (n = 27)	4.6 ± 3.4	6.7 ± 6.6	1.8 ± 2.0[c]
Other Rx (n = 44)	4.3 ± 5.3	0.8 ± 5.7	0.2 ± 1.6

[a]Treatment given during hospitalisation as episodes of monotherapy; patients could have >1 treatment episode per hospitalisation; [b]from start to end of treatment; [c]1 patient treated with normal saline and 1 with tolvaptan had [Na^+] increase >12 mEq/L within 24 hours of treatment.

Implications for clinical practice

Christian Grohé from the ELK Thorax Center Berlin, Germany, one of the study investigators, discusses the implications of these findings, and how he personally manages hyponatraemia secondary to SIADH in SCLC.

The views below are those of the author, and do not necessarily reflect those of the study investigators/study sponsor.

"A good quality of life and avoiding unplanned hospitalisation are of the utmost importance for patients with SCLC. Hyponatraemia can have a very detrimental impact on these factors, and it is not uncommon in SCLC. Therefore, close monitoring for hyponatraemia in SCLC is appropriate.

*In all cases of hyponatraemia in lung cancer, it should be determined whether the diagnosis is SIADH. If SIADH is the cause of hyponatraemia, an active pharmacological intervention should be established as soon as possible. We use hypertonic saline in acute onset or severe SIADH-related hyponatraemia with relevant clinical neurological symptoms. For patients with mild-to-moderate hyponatraemia secondary to SIADH, treatment with Samsca® (tolvaptan) is appropriate as its effects in the treatment of hyponatraemia secondary to SIADH have been demonstrated in clinical trials.**

The effective management of hyponatraemia in SCLC improves the well-being of our patients."

*Studies have shown that Samsca® provides significant improvement in hyponatremia and improves physical functions in patients with SIADH[8]

Conclusion

Hyponatraemia is common in SCLC, and can have a significant impact on patients. Tolvaptan provides an oral, mechanism-based, option for correcting hyponatremia caused by SIADH.[1]

References and prescribing information appear overleaf

Conference News

Are you organising an annual meeting or conference which you would like to tell our readers about?
Or would you like to write a report on a meeting or conference of particular interest?
If so, contact Patricia McDonnell at Oncology News on
T/F: +44 (0)288 289 7023,
E: patricia@oncologynews.biz

European Society for Medical Oncology Congress 2013

Date: 27 September – 1 October 2013. **Venue:** Amsterdam, the Netherlands.

During the current era of rapidly changing scientific knowledge and hope, cancer patients can naturally expect multidisciplinary health care (MDHC). However, the delivery of any meaningful MDHC can be extremely challenging due to limited resources and professional attitudes. The first step to achieve the desired goals has to be to recognise the hurdles and truthfully attempt to take the corrective measures sooner rather than later. At the recently concluded European Society for Medical Oncology (ESMO) meeting in Amsterdam, there were a host of presentations to address these issues. Practice changing data were presented from multiple ongoing trials using surgery, radiotherapy, chemotherapy and molecular agents showing a promising future and reinforcing the multidisciplinary approach in the fight against a variety of cancers. These results are also posing a new challenge of quality assurance and stimulating widespread debates about the value of clinically meaningful endpoints like response rate, progression free survival and frequently only small overall survival gains. With increasing demand and ever decreasing resources, licensing new drugs and evaluating the cost of treatment are the other challenges that need frequent resolution all over the world.

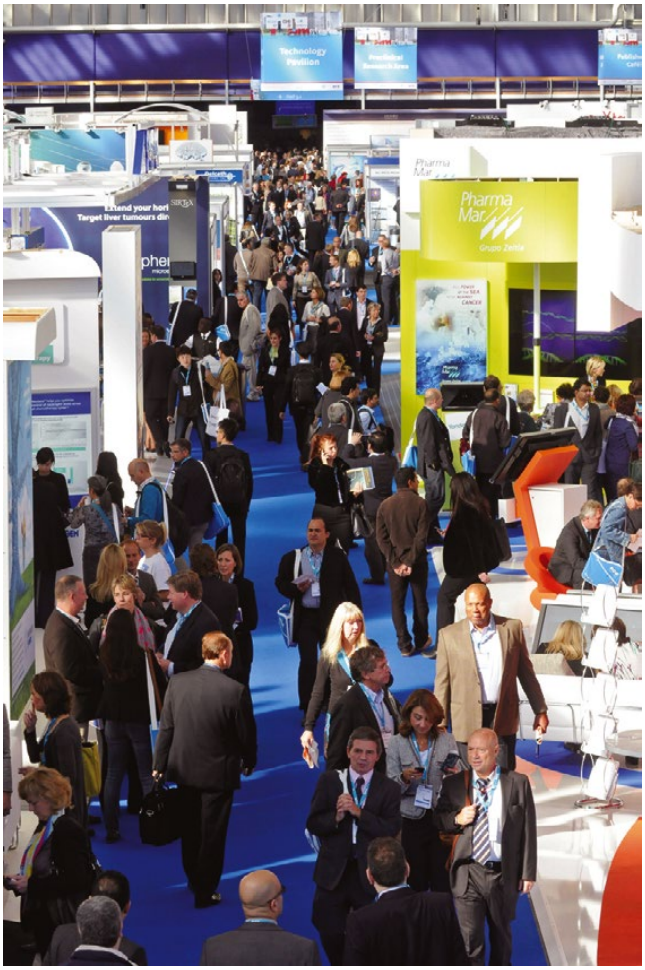
There is growing interest in the research using therapeutic vaccines and immunotherapy in the management of a variety of cancers. Modest clinical benefits reported from recently completed trials using agents like MAGE-A3 (melanoma & lung cancer), Sipuleucel-T (metastatic prostate cancer) have rejuvenated the enthusiasm in the search for understanding their mechanism of action and clinical use. Most tumours use TGF-β to hide from the immune system. The TGF-β is known to inhibit T cell, B cell, dendritic cell and immune effector cell activation. Antigen-loaded dendritic cells activate immune effector cells and once activated they can target and destroy malignant cells despite the continued presence of TGF-β. Locally advanced and metastatic non-small lung cancer has proven to be a difficult area for immunotherapy. In the past several large trial results have generated disappointment despite theoretical opportunities. The results of a phase III placebo controlled multicenter clinical trial on the use of belagenpumatucel-L a therapeutic tumour cell vaccine (Lucanix) was presented by Dr Giuseppe Giaccone from NCI during the presidential session. In this trial, 532 stage IIIA, IIIB & IV NSCLC patients were randomised to receive 18 months of intra-dermal monthly injections followed by 2 quarterly injections of this

experimental agent (n=270) vs placebo (n=262) following completion of their front line chemotherapy. The primary end point was OS and the secondary end points were PFS, objective response rate and safety. The results presented showed that the primary end point of improvement of the median OS was not met (vaccine 20.3 vs control 17.8 months) mainly due to the inclusion of many patients more than 12 weeks after completion of their chemotherapy. However, in patients enrolled within 12 weeks of chemotherapy, a median survival of 20.7 months was observed for the vaccine compared to 13.4 months for the control arm (HR 0.75, p=0.083). Similarly, in patients with squamous cell carcinoma histology, a median survival of 20.7 months was observed for the vaccine compared to 12.3 months for the control (HR 0.58, p=0.092). In the predefined subgroup of patients who received radiation therapy prior to enrolment a median survival of 40.1 months was observed for the vaccine compared to 10.3 months for the control (HR 0.45). These encouraging prospective results in a selected subset of patients support further research on the role of this vaccine in NSCLC. (LBA2).

Dr Soria from France presented one of the most exciting data on the use of intravenous administration of anti PD-L1 antibody in the management of lung cancers though there were few other cancers like renal cell carcinoma and malignant melanoma in this phase I study. The results from this study showing prolonged disease free survival adds to the evidence we have been getting on the use of antibodies in various tumour types. Blockage of various immune targets using agents like PD-1, PD-L1 and CTLA4, which are different to vaccines, is turning out to be a popular area of research. Suppression of the immune mechanism which could favour tumour growth and proliferation is a new mechanism of tumour control. Though these agents take time to see the response and final benefits, Dr Soria presented very nice CT illustrations to show that there is strong carry over effect leading to ongoing tumour shrinkage even after discontinuation of the therapy agent.

There was a 23% objective response rate with 17% achieving stable disease for 24 weeks or longer and a progression free survival rate of 45%. The best response rates were seen in patients with the highest expression of the targeted protein, PD-L1. In patients with increased PD-L1 expression (IHC), the overall response was 83% suggesting that it might be a potential biomarker for response. Fortunately, striking durable responses were seen even in current and past smokers from this novel agent (MPDL 3280A) with limited toxicities. Most of the adverse events seen in this trial were grade 1 or 2 and did not require any intervention. Almost all (95%) patients had brain metastasis. Actually, phase II trials are already in place and many more planned using MDPL3280A as a single agent as well as in combination with other molecular agents in many other malignancies. Similarly, other drugs like EGFR & ALK inhibitors, AP26113, the ARIAD drugs are also looking like they might have a promising future. (Abs. 3408).

During the last decade, the landscape of the HER2 positive breast cancer tumours, which used to carry extremely poor prognosis, has changed considerably. Routine use of anti-HER2 agents like trastuzumab in the neo- & adjuvant setting has become the norm because of substantial improvements in their outcome from its use. Unfortunately, many patients still relapse and retreatment with trastuzumab or lapatinib with or without cytotoxic agents in the second line or beyond results in limited PFS gains. Therefore, there is an ongoing search for newer agents with different targets, mechanism of action or mode of drug delivery with encouraging success with agents like pertuzumab and T-DM1. The results of the phase 3 EMILIA study in patients with HER2-positive locally advanced and metastatic breast cancer



previously treated with a taxane and trastuzumab demonstrated superior PFS and OS and better toxicity profile compared with capecitabine plus lapatinib arm. Based on the EMILIA results, T-DM1 has been approved in several countries. However, T-DM1 has not been previously studied in patients who have received prior treatment with both trastuzumab and lapatinib for advanced disease. The results of the TH3RESA study on the use of T-DM1 in advanced breast cancer patients who have progressed following prior treatment with trastuzumab, lapatinib and a taxane was presented at ESMO2013. Patients were randomised to receive either T-DM1 alone (n=400) or treatment of physician's choice (n=200) till progression. The PFS result by investigator assessment was found to be 6.2 months compared to 3.3 months for the TPC arm. (HR 0.528, p<0.0001). The first interim OS analysis favoured T-DM1 but efficacy stopping boundary has not crossed yet compared to 14.9 months in the TPC arm (HR=0.552, p=0.0034). 44 patients in the TPC arm received crossover T-DM1 treatment after documented progression. The overall response rate in patients with measurable disease was 8.6% in the control arm compared to 31.3% in the T-DM1 arm (p<0.0001). Similarly, there were fewer grade ≥ 3 adverse effects with T-DM1 (32.3%) vs TPC (43.5%), fewer discontinuations and dose reductions due to adverse events with T-DM1. These data reaffirm the results from the EMILIA study, demonstrating a consistent superior benefit with T-DM1 in patients with previously treated HER2-positive advanced breast cancer. (LBA 15). ■

Dr Sunil Upadhyay,
Consultant Clinical Oncology,
Queen's Centre for Oncology & Haematology, Hull, UK.

gliolan® 30 mg/ml powder for oral solution.
Qualitative and quantitative composition: One vial contains 1.17 g of 5 aminolevulinic acid (5-ALA), corresponding to 1.5 g 5 aminolevulinic acid hydrochloride (5 ALA HCl). One ml of reconstituted solution contains 23.4 mg of 5 aminolevulinic acid, corresponding to 30 mg 5 aminolevulinic acid hydrochloride (5 ALA HCl).
Therapeutic indications: gliolan is indicated in adult patients for visualisation of malignant tissue during surgery for malignant glioma (WHO grade III and IV).
Posology and method of administration: This medicinal product should only be used by experienced neurosurgeons conversant with surgery of malignant glioma and in-depth knowledge of functional brain anatomy who have completed a training course in fluorescence-guided surgery. The recommended dose is 20 mg 5 ALA HCl per kilogram body weight.
Contraindications: Hypersensitivity to 5-ALA or porphyrins; acute or chronic types of porphyria; pregnancy.
Undesirable effects: Adverse reactions observed after the use for fluorescence-guided glioma resection are divided into the following two categories: Immediate reactions occurring after oral administration of the medicinal product before anaesthesia (= active substance-specific side effects); combined effects of 5 ALA, anaesthesia and tumour resection (= procedure-specific side effects).
Substance-specific side effects: *Uncommon:* Hypotension; nausea, photosensitivity reaction, photodermatosis.
Substance-specific 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:* Hypotension. *Very rare:* Hypesthesia; diarrhoea. One case of moderate chills; one respiratory insufficiency after overdose, which resolved completely.
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Marketing authorisation holder: medac GmbH, Fehlandtstraße 3; D-20354 Hamburg.
Date of revision of text: 07/2012.
gliolan has been authorised in all countries of the EU as well as in Iceland, Norway and Taiwan

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Changes to the Editorial Board

We have a few changes to the Editorial board, firstly Willie Stewart is stepping down as Assistant Editor for Neuro-oncology, and he has been succeeded by Professor Geoff Pilkington. There are also two new sections in this issue, the first, Image Analysis, which will be co-ordinated by Dr Constantino Carlos Reyes-Aldasoro. The second new section covers Head & Neck Oncology which will be co-ordinated by Mr Mriganka De.

Neuro-Oncology

Professor Geoff Pilkington will succeed Willie Stewart as Assistant Editor – Neuro-Oncology. Geoff has spent his entire career in brain tumour research, having started work on chemical neuro-carcinogenesis where he studied brain cancer stem cells and brain tumour development at the Middlesex Hospital Medical School in the early 1970s and subsequently spent 23 years at the Institute of Psychiatry, King's College, London, latterly as Professor of Experimental Neuro-oncology. In 2003 he moved to the School of Pharmacy & Biomedical Sciences, Institute of Biomedical and Biomolecular Sciences, University of Portsmouth, as Professor of Cellular & Molecular Neuro-oncology. He is Head of the Brain Tumour Research 'Centre for Cellular and Molecular Neuro-oncology' at Portsmouth as well as being immediate Past President of the British Neuro-oncology Society and currently an Executive Board Member of the European Association of Neuro-oncology. He had also previously served for a number of years on the Committee of the British Neuropathological Society as Programme Secretary.

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 as well as development of novel strategies for mitochondrial mediation of apoptosis in glioma, delivery of agents across the blood-brain barrier and genetic regulation of metastatic spread of cancers to the brain. He has successfully supervised 31 PhD students as well as examining another 33 at various universities within the UK and Europe. He has acted as a reviewer for 55 different scientific/medical journals and is currently on the editorial board of four international journals. In addition, he has been a reviewer for 26 UK grant giving bodies and 8 overseas bodies. He is currently on the cancer grants review panel for the Norwegian Research Council and is a member of the scientific advisory board for Children with Cancer UK. He is also a regular attendee at the quarterly All Party Parliamentary Group meetings on Brain tumours at Westminster and three years ago established the South of England Brain Tumour Alliance which brings together seven centres across the region where brain tumour research, diagnosis and therapy is carried out in order to maximize research data from minimal tissue and cell resources and to fast track lab-based research towards translational medicine and clinical trials. He lives on the Isle of Wight and commutes daily across the Solent to his Portsmouth laboratories. In his spare time he lists his major interests as: rugby union, cricket, real ales, seafood and the Greek Islands.

To suggest articles you'd like covered in this section
E: Geoff.pilkington@port.ac.uk

Image Analysis

Dr Constantino Carlos Reyes-Aldasoro (BS UNAM-Mexico, MSc Imperial College, PhD Warwick) 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 (light, fluorescent, confocal, and multiphoton) to the analysis of biomedical datasets such as magnetic resonance, computed tomography and microscopy to advanced computer programming and website development. These skills have been assembled through strategic appointments in technical and life sciences departments. This interdisciplinary approach has enabled him to contribute in different areas of biomedical research, in particular of Cancer, Microcirculation and Inflammation as well as in Engineering and Computer Science. He is an elected member of the Executive Committee of the British Association for Cancer Research and chair of the Conference Medical Image Understanding and Analysis in 2014. In the Image Analysis section he wishes to highlight the huge potential of interdisciplinary research and the contribution of image analysis to oncology.

To suggest articles you'd like covered in this section
E: reyes@city.ac.uk

Head & Neck Oncology

Mr Mriganka De is a Consultant ENT/Head and Neck surgeon at Royal Derby Hospital. He underwent basic surgical training in South Wales, higher surgical training in West Midlands and completed his sub-speciality training in Head and Neck Oncology in Amsterdam, Birmingham and Glasgow. His current sub-specialty interests are Transoral Laser Microsurgery, Thyroid and Parathyroid surgery. Mr De has been involved in several national ENT/Head and Neck courses, and has published many papers and articles on head and neck cancer with particular focus on management of early laryngeal cancers. In addition to presenting at international meetings, he has been on the faculty of several head and neck courses and is one of the co-founders and organisers of the Midlands Laryngeal Surgery Course, Derby and West Midlands ENT Emergency Course, Birmingham. Mr De is an Honorary Senior Research Fellow at University of Birmingham and has been involved in epigenetic research at University of Birmingham.

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Professor Geoff Pilkington
EANO Executive Board Member.
Professor of Cellular & Molecular Neuro-oncology, School of Pharmacy & Biomedical Sciences, University of Portsmouth
St Michael's Building, White Swan Road, Portsmouth, UK.

Correspondence:
E: geoff.pilkington@port.ac.uk

Neuro-oncology in the UK, Europe and beyond; the role of EANO

In July this year, having completed two years as President of the British Neuro-oncology Society (BNOS), I handed over, and with some degree of relief (since this is a time consuming as well as rewarding role) because I could get back to spending more time with my own research team but also because I had every confidence in my successor and friend, Professor David Walker, in continuing and nurturing the professional development of BNOS.

My association with BNOS has been long-standing, indeed from its very origins in 1980 and its first annual conference in 1981, initially under the name of the British Glioma Group. BNOS, however, is more than a UK-wide organisation aimed at communication between individuals from various disciplines who share a common professional interest in tumours of the nervous system. Indeed, it started a trend for similar societies and associations to be formed in a number of other European nations. It should be said that a similar model was set up some years earlier in the USA by UCSF neurosurgeon Charles Wilson, although this was only a vehicle for annual meetings and this was organised on an invitee only basis. This format became known as the 'Asilomar' series of conferences and, indeed, is still active today under the banner of the series of 'International Conferences on Brain Tumor Research and Therapy', the next of which will be held at Lake Tahoe, California in the Spring of 2014.

In Europe, by the beginning of the 1990s small groups of brain tumour researchers and clinicians were meeting informally at various other conferences to discuss the merits of a pan-European organisation which would primarily hold multidisciplinary neuro-oncology conferences. Following a, now historic, meeting in Pommersfelden, Bamberg, Germany, in 1994 the European Association of Neuro-oncology (EANO) was established as a multidisciplinary society devoted to Neuro-oncology with its administrative base in Brussels. In the same year, the first EANO Congress was held in Maastricht with 180 participants. Today EANO has over 748 members from more than 30 countries, in Europe and across the world (North America, Asia and North Africa). To date, EANO has organised nine biannual Scientific Congresses: Maastricht in 1994, Würzburg in 1996, Versailles in 1998, Copenhagen in 2000, Florence in 2002, Vienna in 2006, Barcelona in 2008, Maastricht in 2010 and Marseille in 2012). In addition, a joint EANO/World Federation for Neuro-Oncology Conference was held in Edinburgh in May 2005. EANO is part of the World Federation of Neuro-Oncology, which is comprised of EANO, the Society of Neuro-oncology (SNO) which represents North America and Asian Society of Neuro-oncology (ASNO), which represents member nations from throughout Asia.

Today, EANO represents all clinical and scientific disciplines involved in the research, diagnosis and treatment of primary tumours of the nervous system and of neurological complications of extra-neural cancers. The interest in CNS tumours is increasing due to developments in molecular biology, neuroimaging and treatment options, including lower toxicity and targeted therapeutics. EANO now co-operates with the various national Neuro-oncology societies throughout Europe. This is facilitated by a recently constituted specific committee composed of Presidents/Chairs of the national Societies/Associations/Groups, which meets during the bi-annual EANO congresses to stimulate international co-operation in research and clinical training and practice.

EANO stimulates interaction and co-operation within a multidisciplinary society with varied educational programs. Competitive grants are offered for EANO Congress attendance, as well as for visits to departments and clinical fellowships. Like BNOS, EANO Congresses also include an Educational Day. An additional, EORTC-EANO-ESMO educational meeting is held biannually in Eastern Europe. EANO is also a member of the European CanCer Organisation (ECCO) and is involved in the educational programmes and an accreditation system. A common EU project with ECCO on oncological investigations has also been implemented.

EANO Congresses are organised every other year. Scientific and educational programs as well as invited speakers delivering "state of the art" lectures make up the core programme. There are also sessions for nurses and related health groups and meetings with members from the new European countries and North Africa. Proffered papers and posters cover all scientific fields of Neuro-oncology. The EANO website offers current news on Neuro-oncology, and monthly case discussions for continuing medical education are offered.

The EANO Board, which consists of professionals from the different specialities within the field of Neuro-oncology, is elected biannually, while the Scientific Committee is involved in compiling the congress programmes and also provides advice in scientific matters. Open positions for all positions of EANO are regularly announced on the website. At the AGM of the last EANO conference in Marseille (2012), I was elected to the Executive Board of the Association, having previously served on the scientific board several years earlier. In this capacity I hold joint responsibility, with Professor Martin Taphoorn (The Hague, Netherlands) for Education and, as a scientist member, represent and foster the enhancement of scientific endeavour in the activities of

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References:

1. VIMPAT® Summary of Product Characteristics.

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EANO. To these ends Martin and I are expanding education opportunities for the EANO membership within the field of Neuro-oncology. This includes provision and extension of the bursary scheme and fostering relationships with financially less advantaged regions of Europe to integrate them into our programme of activities.

Under the present leadership of Professor Riccardo Soffietti (Turin), the President of EANO, a number of recent changes to EANO have facilitated further professionalization and efficiency. The EANO office is now located in the Vienna Medical Academy buildings in Austria where an excellent team provide a highly professional and efficient service to the Association. Re-branding to refresh the look of EANO and all EANO documents with a unified brand and logo is also in progress to include re-launching the website- making it more user-friendly and up to date on issues within Neuro Oncology. The open access EANO Magazine for EANO members was also launched under the editorial guidance of immediate Past President of EANO, Professor Wolfgang Grisold (Vienna) which provides a range of topical presentations on highly readable key research and clinical areas of the discipline. ■

With regard to the Neuro-oncology conference agenda, the 4th Quadrennial meeting of the World Federation of Neuro-oncology will be held in conjunction with the 2013 Scientific meeting and Education Day of the Society for Neuro-oncology in San Francisco on 21-24 November 2013 (http://www.soc-neuro-onc.org/2013-world-federation-mee/). The next BNOS conference, Contemporary Approaches to Paediatric and Adult Brain Tumours will be held at Liverpool John Moores University's Art and Design Academy on 9th-11th July 2014 (http://www.bnos.org.uk/conference.html) and the 11th EANO Congress will be held in Turin, Italy in October 2014. Further information is available on the EANO website: www.eano.eu.

Membership of the Association is paid biannually and, if you are not already a member of SNO, offers the added benefit of a free subscription to the key journal of our discipline, Neuro-oncology (IF is currently 6.180).

Membership or general enquiries can be made either through the EANO website of by contacting:

Eileen Smith, M.A. | EANO Office
Vienna Medical Academy
Alser Straße 4
A-1090 Vienna Austria
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Cancer Image Analysis

Constantino Carlos Reyes-Aldasoro,
Lecturer in Biomedical Image Analysis
School of Engineering and Mathematical Sciences
City University London
London, UK.

Correspondence:
E: reyes@city.ac.uk

Welcome to the first in a series of articles that will highlight the role of image analysis in oncology. Cancer Image Analysis (CIA) is concerned with the extraction and manipulation of useful information from oncological images, and therefore it is closely related to Cancer Imaging per se and can be seen as complementary step in the process towards diagnosis, screening, drug testing or assessing treatments. CIA is a very wide field of research, not only due to the wide range of cancer-related images, from MRI to histology to optical images, but also because image analysis has inherited many techniques from the fields of Statistics, Pattern Recognition and Computer Vision. This series will show the potential of image analysis as applied to cancer with the ultimate objective of fostering an interdisciplinary cross-fertilization that will bring benefits to clinicians, scientists and ultimately the patient.

Introduction

Technological advances in imaging and computers are seen in everyday life. Digital cameras are widely used as they have become cheaper and smaller, yet offer very high quality. Computers have also become more powerful, less expensive and easier to handle. The advances in storage technology in the form of optical disks (CDs and DVDs), magnetic disks (Internal and External Hard Disk Drives), flash memory data storage device (USB drives) and even the availability of some of these technologies through the internet (storage area networks) have grown accordingly. Large files can be transmitted around the globe through the internet without the need for specialised equipment or skills.

In the life sciences and medicine, conjunction of imaging technology with computers that control cameras, microscopes and other equipment have resulted in new technological setups that generate very large amounts of images or videos at a speed that was unimaginable a few years ago. However, once the imaging has been completed, there is sometimes a lack of resources to process, quantify, analyse and interpret the wealth of the information contained in them. In many cases data is acquired at a faster rate than the processing rate of human experts; this situation has increased the workload of pathologists and radiologists in both clinical [1,2] and experimental settings [3], for instance, in biomarker discovery. This situation has led great opportunities in the field of Biomedical Image Analysis (BIA).

The research in BIA is intrinsically interdisciplinary as the expertise required for processing images is largely computational and mathematical. However, all the algorithms or methodologies are tailored to the physical characteristics that form an image in a biomedical or clinical study, and these characteristics are in turn related to anatomy, physiology, chemistry and their underlying biology. Therefore, imaging and image analysis are linked by the data, the images themselves, and the nature of the data. The fields diverge once the data has been acquired; traditionally, specialists like pathologists or radiologists observe the images to reach a conclusion, based on the superb capabilities of human vision and highly specialised training. Image analysis uses computers and digital image processing techniques.

Image analysis methodologies can assist experts in three ways. First, computers are highly efficient at processing large amounts of data; when a study requires the comparison of two sets, each with hundreds of images, a computer shortens the time required to detect any possible difference. Second, algorithms may not be as good as a visual examination by an expert, but they are consistent and therefore avoid the well-known problem of inter- and intra-observer variability. Third, and probably most important, there may be information not immediately apparent to a human eye that can be extracted through computer algorithms, patterns or texture that, for instance, can help an expert reach a conclusion.

Elements of Image Analysis

There are many ways in which image analysis work can be classified, one of the most common being to group into organ-specific topics, as the techniques applied to the heart or the brain will share anatomy, physiology, and sometimes imaging technique. Another way to classify research is through acquisition technology used to take images: Microscopy, Computed Tomography, Magnetic Resonance Imaging or Spectroscopy, etc. Yet another possibility is through the underlying algorithms or techniques used to process the images, like Fractals, Texture or Registration. These divisions are naturally not clear-cut; mammography, for instance, is related to an organ and an acquisition technique.

When a cancer-related image is analysed, one or more steps can follow each other. The steps are related to what is done with the images, regardless of the acquisition technique, organ or disease. Some common steps are described below and illustrated in Figure 1.

The analysis generally starts with an enhancement step. Biomedical images can be noisy, with low contrast or complicated due to artefacts such as caused by motion [4] or uneven intensities [5]. It should be noted that enhancement is done on the images, and is not related to the enhancement that can be achieved by modifying the acquisition itself, like using contrast materials [6]. Enhancement techniques modify an image in such a way that it is easier to interpret or analyse. Some of the techniques may be relatively simple, such as stretching a histogram to boost contrast, removing noise through filtering, and correcting shading or uneven intensities. However, in some cases, enhancement may become rather involved, as in compensating for cardiac or respiratory motion that causes errors when planning and delivering radiotherapy treatment for lung [7] or colon cancer [8]. Enhancement should therefore be understood beyond the transformations that create a visually improved image from a human perspective. It is also important to consider that the enhancement of the visibility of features – calcifications for instance – may distort the shapes of these or other features that ultimately could lead to an incorrect diagnosis if the variations are not taken into account [9].

A segmentation step aims to partition an image into regions or classes that are homogeneous according to certain criteria. Thus, an image can be separated into one or more objects and a background. The objects may or may not correspond directly to an anatomically-relevant structure (an organ), a subset of a structure (a tumour), or a feature of a structure (the cell membrane). There are many segmentation techniques,

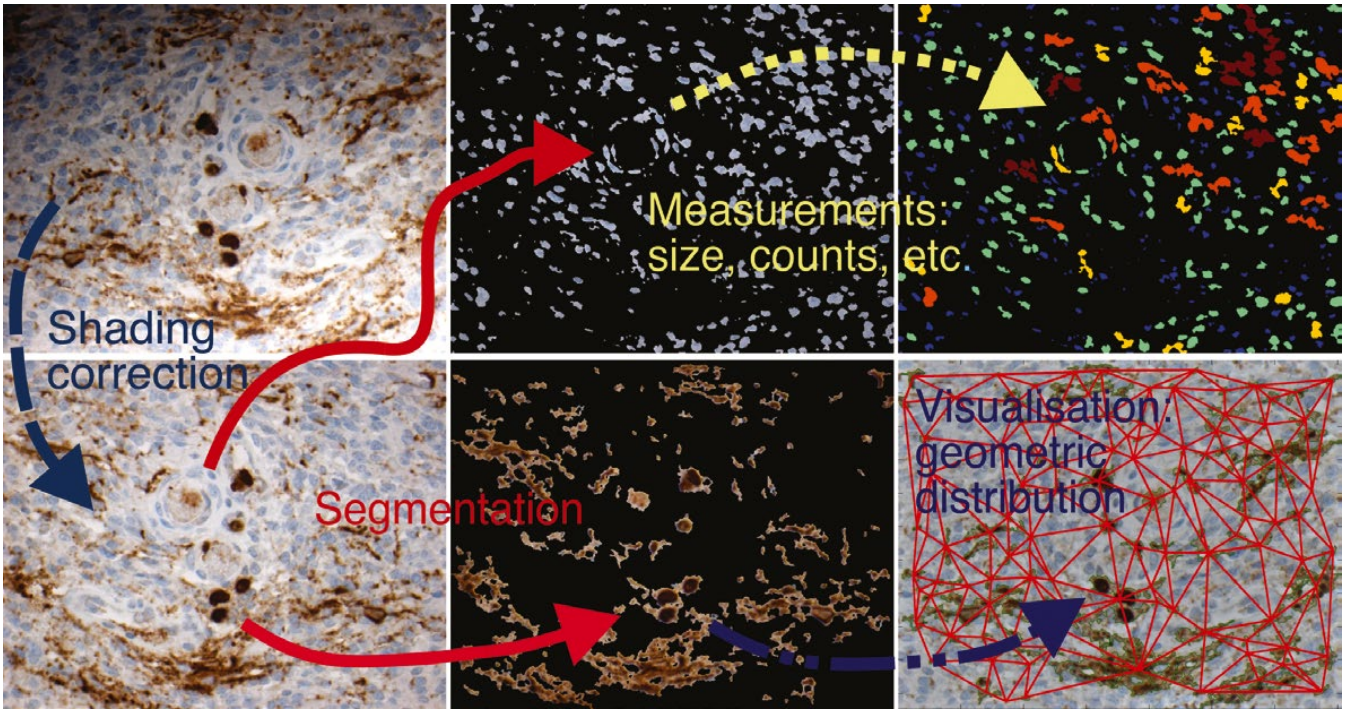

Figure 1: Illustration of several image-processing steps. An image obtained by immunohistochemistry is first enhanced to remove inhomogeneous shading seen in the upper part of the image. The corrected image is then segmented into two types of cells using chromatic information. Once the cells have been segmented into objects at this stage, numerous measurements can be made - size, elongation, density, variation of intensity, etc. In this example, blue cells are colour-coded according to their size: brown > orange > yellow > green > blue. Some measurements, e.g. the geometric distribution of the brown cells, can be used for visualisation purposes.

one of the most traditional segmentation techniques being to assign pixels to different classes by comparing their intensities against a value or a threshold (referred to as thresholding). Even when thresholding is very simple, it can be effective in the analysis of prostate malignancies [10]. Other techniques can: look for edges on images, for instance to delineate the breasts as areas of interest in thermal imaging [11], compare structures, like spiculated lesions, against pre-defined models in mammography [12], or perform regional analysis of the intensities of the pixels, in terms of their texture to segment cancerous and normal regions of colon biopsies [13], or lesions and normal brain tissue [14]. In some cases, a combination of different algorithms is necessary to obtain satisfactory segmentation; this is common in immunohistochemistry [15,16]. In PET, it is of particular interest to delineate tumour volumes, which can be achieved by setting thresholds based on the SUVmax, measuring the local contrast or measuring the gradient of the intensity [17].

At the measurement step, a series of rules are applied to extract numerical values from the images, which may have previously been processed with other steps. It is possible to apply a very large number of rules, with a filter bank for instance, and create a large measurement space (sometimes called pattern representation) with the result of all the rules. Some of these measurements may be directly related to a cancer condition - the irregular border shape of a melanoma [18] or the effect of a drug. The length of microvessels and their characteristic colours are related to the influence of vascular disrupting agents [19]. In the histology of cancer, the number of cells or nuclei can sometimes have diagnostic significance [20], for instance, the number of tumour infiltrating lymphocytes from thresholded images [21]. Common measurements in sections can include area, size, colour, elongation, and sphericity [16]. The measurements may come from different acquisition modes; the combination of data from MR spectroscopy with textural measurements from MRI has been used to discriminate meningiomas from metastatic brain tumours [22]. However, it is important to note that many measurements may not be of interest and therefore might be discarded in a process called feature selection, or combined among themselves to create new measurements, which is called feature extraction.

At the classification step, the information obtained from the segmentation and measurement steps is integrated in some way, and rules are applied to reach decisions that have clinically or biologically relevant criteria in a particular context. In some cases this step is called computer-aided-diagnosis as it provides information that can be used to reach a diagnosis. For instance, Loeffler [10] presented an algorithm that differentiates Gleason grade 3 from grade 4/5 histology. Rojas-Domínguez [23] analysed breast-mass contours as a step toward breast cancer diagnosis, and Chen [24] presented a method for automated mammographic risk classification based on estimation of breast density.

There is a very fine line between segmentation and classification; indeed the terms are sometimes interchanged. In this review, we consider that the segmentation step is at the level of the pixels and their characteristics: there are 10 regions with pixels above the value of 100, and classification on the other hand, reaches a higher level; e.g. a higher than normal density of cells may indicate the presence of a tumour.

Another step, not necessarily after classification is a visualisation step, where information from different sources may be combined or merged. The most common application of a merging of information in a cancer context is probably the registration between PET and CT modalities [25]. CT provides anatomical information whereas PET provides functional information. The visualisation can be formed with extracted features from a single source; for instance, Ganeshan [26-28] developed an interesting technique that combines texture features with CT scans in the analysis of liver, colorectal and oesophageal cancer.

Image Analysis Tools

Image analysis relies on the use of suitable software tools and ever more powerful computers. Software packages developed specifically for image analysis consist of a basic platform to which modules, sometimes called plug-ins, are added (ImageJ, ICY, Imaris, AxioVision, Volocity, etc.). There are some general purpose scientific platforms that are highly flexible and powerful, offering high-level programming with a wide variety of toolboxes, thus being capable of processing images in a very efficient way (Matlab, Scilab, Octave, Mathematica, etc.). These platforms provide many advantages over lower level programming languages like C and FORTRAN, especially in terms of visualisation, functions and toolboxes, at the expense of slower processing times. There is even the possi-

bility of using graphically-oriented packages (Photoshop, Corel, etc.) to analyse biomedical images; however, this option does not provide the power of the previous cases. Some of these tools are open-source and freely available, but a certain level of software expertise is required to use them effectively in obtaining quantitative results.

With the development of the internet, new possibilities have emerged in which web-based tools are available, for example, in: virtual slide analysis in diagnostic pathology [29], the analysis of microarray gene expression [30], and the online automatic processing of images of several cancer-related experiments [31].

Conclusion

This article briefly describes some elements of image analysis mostly related to oncology. In future issues, different techniques will be described in the context of clinical applications and pre-clinical research. ■

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The Benefits of Biobanking Human Tissue as a Hub for Future Translational Research

Amir Gander,
Tissue Access for Patient benefit (TAPb) manager, at University College London
London, UK.

Mohammed R S Keshtgar, BSc, FRCSI, FRCS (Gen), PhD
Professor of Cancer Surgery and Surgical Oncology
Royal Free London Foundation Trust
University College London
The Breast Unit,
London, UK

Correspondence:
Amir Gander,
E: a.gander@ucl.ac.uk

The pace of translational research has created a need for experimentation on human biological samples. Using such samples can fill the gap between monolayer cell cultures, animal models and testing new treatments in humans, and includes whole organs, tissue, biofluids and their derivatives [1]. Delivery of robust data from these samples relies on providing high quality biospecimens, defined by tissue samples that are linked to detailed records on the tissue collection protocol and allied clinical information, stored in a secure pseudoanonymised format. The parameters that constitutes high quality biospecimens are set by the requirements of advancing experimental techniques and key regulatory stipulations. The 2007 European Union Tissue and Cells Directive and the UK 2004 Human Tissue Act (HTAct) set the regulatory framework and have resulted in a climate where biospecimens are increasingly processed and stored in large centralised facilities (in place of small local stores) [2]. These facilities take advantage of economies of scale and are better able to meet regulatory requirements and quality needs of researchers. However, the rise of such facilities has presented a number of challenges that can be categorised into three areas: (1) delivery of useable samples to promote translational research; (2) sustainable business models; (3) obtaining informed consent and ethics.

Biobank model

A common biobank model involves collecting a biospecimen from tissue removed during surgery that is surplus to diagnostic requirements, or taken alongside conventional medical testing (e.g. blood and urine). Biospecimens can be used fresh or stored in biobanks, often as fixed blocks or cryopreserved where the specific collection conditions, allied clinical and life style information is linked to each sample. The allied information allows researchers to assess the context of their findings, whilst detailed collection information ensures their data is robust. With well administered and integrated systems, this model can deliver highly quality biospecimens.

Researchers, clinicians and healthcare professionals involved with breast cancer care have recognised the need for high quality biospecimens through biobanking. Until relatively recently, research into BRCA 1 and 2 had primarily focused on investigating the cellular function of the multi-domain proteins, leading to some important new treatments. However, only a small proportion of breast cancers develop due to a loss of BRCA function, mainly resulting from somatic mutations or changes in expression of other genes [3]. Testing on biospecimens could provide a way to relate cellular signalling pathways and changes in beast architecture, spatial, temporal and differential control of gene expression. Data from such experiments can then be linked to other studies, such as DNA analysis from cancer prevention trials and clinical trials for radiotherapy and chemotherapy that link DNA variants to treatment responses [1].

Sharing of the datasets

To facilitate sharing of datasets and to truly realise the translational potential of biobanks, it could be argued that data from researchers should be returned to the biobank and linked to the original biospecimen. Biobanks are perfectly placed to become custodians of both biospecimens and associated datasets, resulting in a significant increase in research value. For example, published trial results from UK, Europe and the US can be complimentary, although there are limitations to accessing robust data from different sources, pointing to a need for greater international exchange of information. Commonly, data on biospecimens are either part of intellectual property or are selectively published in academic journals (i.e. predominantly positive data) [4]. Efforts to share data are already underway, notably the Breast Cancer Tissue Bank established in 2010, which has a two year time limit on returning experimental data on tissue obtained from the biobank [5]. Furthermore, if the resulting data sets are stored in the biobank for later data mining, the research value for each donation can be significantly increased. Encouraging such a system will need buy in from private and public sector researchers, a proposition that requires further exploration, although this is a model under consideration as part of the University College London Tissue Access for Patient Benefit Project.

Sustainability

Returning results and offering high quality biospecimens forms is part of adding value to biobanks that should enable them to become self-sustaining entities, especially in a climate of financial restrictions in healthcare and research. Many standalone biobanks need additional funding to support their activities. Furthermore, there have been cases where biobanks prospectively collect tissue over many years only to discard biospecimens due to the lack of adequate management systems. At the same time many commercial researchers are desperately seeking high quality biospecimens to perform pre-clinical and clinical trial experiments to bring new treatments to market [6]. The future for biobanks may lay in diversification of research activities around centralised infrastructure that benefit from automation and integration to increase efficiency and quality of samples. For example, the efficiency of a single tissue collection can be optimised by using existing facilities associated with healthcare institutions (e.g. histology, biochemistry and clinical trial infrastructure), as well as allowing a number of researchers to perform a whole range of studies on a single set of biospecimens.

Furthermore, the transition from centrally funded biobanks to self-sustainability needs the adoption of business models that can release the research value

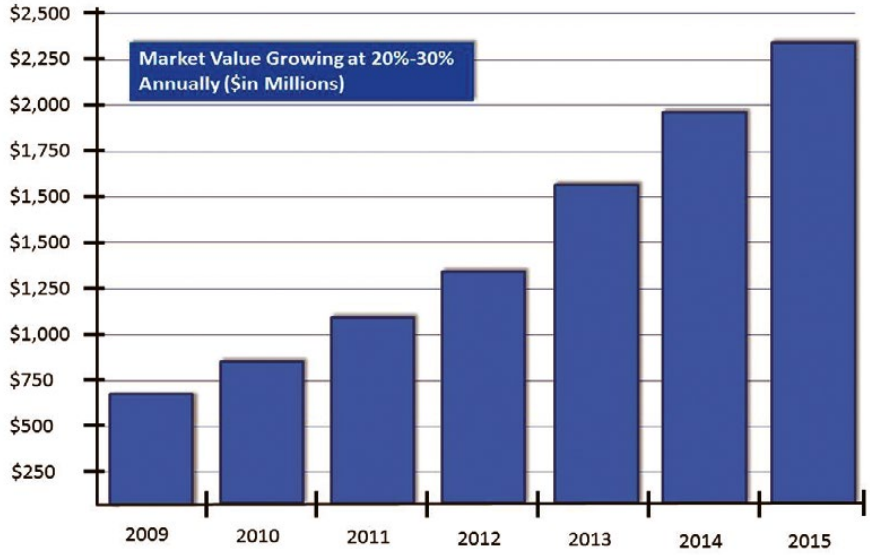

Figure 1: The increase in value of the USA Biobanking Market [7].

within biospecimens and attract private sector researchers as well as academic projects. One option could be to oblige data sharing arrangements, albeit non-commercially sensitive data sharing, where the added research value for biospecimens could lead to more sustainable biobanks. Another important consideration is calculating the true cost of biobanking, for example devising the Total Life Cycle Cost of Ownership (TLCO). Using TLCO the costs of owning, operating and maintaining a tissue provision service is compared against potential income generation by adding research value to biospecimens through diversification of activities and support services. However, the current lack of data on costs and associated outcomes, makes calculating the TLCO difficult. This is mainly due to most biobanks being born out of research department with sustainability as a standalone entity not being the main focus, with many hidden costs paid for by the supporting institution. One encouraging trend that illustrates the potential for biobanks to become self-sustainable is the increasing biobanking market for the use of human tissue in drug discovery and preclinical trials (Figure 1). Many challenges remain, however, owing to the incredibly fragmented nature of the industry exemplified by no one institution having more than 3% share of the biobanking market in the US. There is also a lack of standardised collection and storage protocols quality or data integrity [5,7].

Ethical issues and consent

With expanding use of biospecimens and associated data there is clearly a need for researchers and biobanks to ensure patients are actively involved with these developments. The 2004 Human Tissue Act (HTAct), National Ethics Review Service and the Nuffield Council of Bioethics approve of researchers obtaining generic consent from patients to use their tissue for future ethically approved research. The process involves prospectively collecting biospecimens to be held within a licensed biobank, for researchers to then apply to the biobank for ethical approval to use the samples [2,8]. There are critics of generic consent, describing it as not being truly "informed" consent (a stipulation of the HTAct) as the future research cannot be defined, therefore suggesting alternatives such as opt-in and tiered consent [9].

Opt-in consent involves asking the patient whether they would allow their tissue to be used for a specific research project. Each additional project would need the researcher to approach the patient for renewed consent. The main disadvantage is the potential for valuable biospecimens to be discarded after a research project ends, thereby increasing the cost to output ratio of the research project.

Alternatively, tiered consent is a more restricted form of generic consent that allows the donor to agree to the use of their samples in unknown future projects, but gives the option of specifying particular categories of research that they wish to exclude, e.g. embryonic research or commercial research. Tiered consent can be complex to administer without sophisticated IT systems to track consent. Most licensed biobanks offer a mixture of generic and tiered consent, with many opting to refuse patients who place stipulations over and above what an ethical review board would approve.

Studies surveying UK Adults showed 55% in favour of opt-in consent, although with greater discussion less restrictive models of consent became more acceptable[10]. A similar study across Europe showed between 69-95% support for generic consent (depending on country)[11]. As a whole there is a preference amongst the UK public for on-going choice and control over donated biospecimens. One suggested method of allowing greater involvement is to create a Wiki style governance structure, where the biobank governance policies would be made available online, for any registered participants to modify and discuss on an online forum. Once a consensus has been reached a biobank committee would act as final arbiters to decide whether the policies are scientifically, ethically or legally valid[12].

The biobanking sector is at the beginnings of an exciting journey towards forming the cement between platforms used in translational research. As they develop and expand, involving all the stakeholders for research using human tissue is crucial in ensuring sustainability and increased research value. The most important stakeholder is the patient or volunteer who must maintain trust in the system, a challenge that can only be tackled through robust informed consent pathways and public awareness campaigns and total transparency. ■

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STRENGTHEN HER PROTECTION

PERJETA is indicated for use in combination with Herceptin® (trastuzumab) and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease.[1]

Is it time to give her more than Herceptin and chemotherapy?

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pertuzumab
strengthen HER2 suppression

PRESCRIBING INFORMATION
PERJETA® (pertuzumab) 420 mg concentrate for solution for infusion
Indications: In combination with trastuzumab and docetaxel for the treatment of adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease **Dosage and Administration:** Please refer to Perjeta Summary of Product Characteristics (SmPC) for full guidance. Patients treated with Perjeta must have HER2-positive breast cancer, defined as a score of 3+ by immunohistochemistry (IHC) and/or a ratio of ≥2.0 by in situ hybridisation (ISH) assessed by a validated test. The loading dose is 840 mg administered as a 60 minute intravenous (IV) infusion, followed 3-weekly by a maintenance dose of 420mg administered over 30-60 minutes. When administered with Perjeta the recommended loading dose of trastuzumab is 8mg/kg body weight administered as an IV infusion followed 3-weekly by a maintenance dose of 6mg/kg body weight. When administered with Perjeta the recommended dose of docetaxel is 75mg/m2, administered on a 3-weekly schedule. The dose of docetaxel may be escalated to 100mg/m2 on subsequent cycles if the initial dose is well tolerated. The products should be administered sequentially. Perjeta and trastuzumab can be given in any order. When the patient is receiving docetaxel, this should be administered after Perjeta and trastuzumab. Perjeta should be administered by a healthcare professional prepared to manage anaphylaxis and in an environment where full resuscitation service is immediately available. **Contraindications:** Hypersensitivity to Perjeta or to any of the excipients. **Precautions:** Please refer to the Perjeta SmPC for further information. Decreases in left ventricular ejection fraction (LVEF) have been reported with products that block HER2 activity, including Perjeta. Perjeta has not been studied in patients with: a pre-treatment LVEF value of ≤50%; a prior history of congestive heart failure; LVEF declines to <50% during prior trastuzumab adjuvant therapy; or conditions that could impair left ventricular function. Patients who have received prior anthracyclines or prior radiotherapy to the chest area may be at higher risk of LVEF declines. Assess LVEF prior to initiation of Perjeta and every 3 cycles during treatment. If LVEF is <40% or 40-45% associated with ≥10% points below the pretreatment value, Perjeta and trastuzumab should be withheld and a repeat LVEF assessment performed within approximately 3 weeks. If the LVEF has not improved, or has declined further, discontinuation of Perjeta and trastuzumab should be considered. Perjeta has been associated with infusion and hypersensitivity reactions. Close observation of the patient during and for 60 minutes after the first infusion and during and for 30-60 minutes after subsequent infusions is recommended following Perjeta administration. If a significant infusion-reaction occurs, the infusion should be slowed down or interrupted and appropriate medical therapies administered. Patients should be evaluated and monitored until resolution of signs and symptoms. Perjeta must be permanently discontinued in case of NCI-CTCAE Grade 4 hypersensitivity reactions (anaphylaxis), bronchospasm or acute respiratory distress syndrome. Patients treated with Perjeta, trastuzumab and docetaxel are at increased risk of febrile neutropaenia compared with patients treated with trastuzumab and docetaxel, especially during the first 3 cycles of treatment. In the pivotal trial CLEOPATRA no events of febrile neutropaenia were reported after docetaxel cessation. **Drug Interactions:** No pharmacokinetic interactions were observed between Perjeta and trastuzumab, or between Perjeta and docetaxel in a sub-study of 37 patients in the pivotal trial. **Pregnancy and Lactation:** Women of childbearing potential should use effective contraception while receiving Perjeta and for 6 months following the last dose of Perjeta. A decision should be made to discontinue breast-feeding or to discontinue treatment taking into account the benefit of nursing for the child and the benefit of Perjeta therapy for the woman. **Side-effects:** Please refer to the Perjeta SmPC for further information. In the pivotal clinical trial Perjeta was given in combination with docetaxel and trastuzumab. It is, therefore, difficult to ascertain the causal relationship of an adverse event to a particular product. The safety of Perjeta in phase I and II studies was generally consistent with the pivotal trial, though the incidence and most common ADRs varied depending on whether Perjeta was administered as monotherapy or with concomitant anti-neoplastic agents. In the pivotal trial the most common serious adverse reactions were febrile neutropaenia, neutropaenia and diarrhoea. Fatal outcomes in the pivotal study were mainly due to febrile neutropaenia and/or infection. *Very common reactions:* Upper respiratory tract infection, nasopharyngitis, febrile neutropaenia, neutropaenia, leucopaenia, anaemia, hypersensitivity/anaphylactic reaction, infusion related reaction/cytokine release syndrome, decreased appetite, insomnia, peripheral neuropathy, peripheral sensory neuropathy, headache, dizziness, dysgeusia, lacrimation increased, dyspnoea, cough, diarrhoea, vomiting, stomatitis, nausea, constipation, dyspepsia, alopecia, rash, nail disorder, pruritus, dry skin, myalgia, arthralgia, mucositis/mucosal inflammation, pain, oedema, pyrexia, fatigue, asthenia. *Common reactions:* paronychia, left ventricular dysfunction (including congestive heart failure), pleural effusion, chills. *Laboratory abnormalities:* In the pivotal trial, the incidence of NCI-CTCAE (version 3) Grade 3–4 neutropaenia was balanced in the two treatment groups. **Legal Category:** POM **Presentation and Basic NHS Cost:** Pack of one 14ml (30 mg/ml) glass vial - £2395 per vial excluding VAT **Marketing Authorisation Number:** EU/1/13/813/001 **Marketing Authorisation Holder:** Roche Registration Limited, 6 Falcon Way, Shire Park, Welwyn Garden City, AL7 1TW, United Kingdom PERJETA is a registered trade mark **RXUKMEDI00144(1)** Date of Preparation: **August 2013**

▼This medicinal product is subject to additional monitoring. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44(0)1707 367554.

Reference: 1. PERJETA Summary of Product Characteristics. September 2013. Date of Preparation: September 2013 RXUKPERT00125

Fear of Recurrence: it's time for us to do more for patients

Professor Simon N Rogers,
Consultant Maxillofacial Surgeon, Aintree University Hospital and Evidence-Based Practice Research Centre (EPRC), Faculty of Health, Edge Hill University, Ormskirk, UK.

Gerald M Humphris
Professor of Health Psychology,
Medical School,
University of St Andrews
Honorary Consultant in Clinical Psychology,
Edinburgh Cancer Centre,
Western General Hospital,
Edinburgh, Scotland, UK.

Correspondence:
Professor Simon N Rogers,
Consultant Maxillofacial Surgeon,
Aintree University Hospital and Evidence-Based Practice Research Centre (EPRC), Faculty of Health, Edge Hill University,
St Helens Road, Ormskirk, L39 4QP, UK.

How often do we talk about the fear of the cancer coming back to patients and their carers? The evidence is that we don't raise the issue of fear of recurrence often enough during follow-up and this leads to potentially avoidable anxiety and distress. Fear of recurrence is a very sensitive area but clinicians and the wider professional support network can do more to help patients.

Recent evidence for the Patient Concerns Inventory (PCI) [1] is that in head and neck cancer (H&N) [2] (Figure 1) breast cancer [3] (Figure 2), and neuro-oncology [4], fear of recurrence (FOR) is a key issue that patients wish to talk about in their follow-up clinics. It is the most frequent item in PCI-H&N and PCI-breast cancer. In a survey of 447 H&N cancer patient the frequency varied from 32% following advanced oral cancer to 44% in early oropharyngeal cancer [5]. In a survey of 200 breast cancer patient 49% wanted to discuss fear of recurrence, 31% fear of cancer spreading and 25% fear about the future, with 57% raising one or more of these concerns. It is likely that FOR is a concern common to all cancers [6] and that these fears are formed early in treatment. In the past we just have not been able to identify the issue very easily as it is hard to raise the topic in clinic without a prompt from the patient. It tends to be a taboo subject and the simplest way the patient and the clinician tackle the matter is just not to mention it. Those patients wishing to raise the topic in clinics via the PCI are unpredictable by stage of disease, radicality of treatment, time since treatment, likelihood of recurrence [7,8]. Older patients are less prone to FOR problems. Patients with early H&N cancers treated many years before, though from the clinical perspective have very low recurrence risk, can still have FOR hence there is value in allowing patients to express these concerns via a prompt such as the PCI. Clinicians should not underestimate the reluctance of patients raising this issue with them. Patients seem acutely aware of the pressures that oncology teams are under to deliver cancer care efficiently and therefore do not wish to raise an issue that might delay the clinic schedule. The patient may also feel somewhat ashamed to raise a delicate issue that may challenge the ethos of the treatment strategy functioning as a permanent cure. The discomfort of inspecting a non-ideal result of the care and attention received such as a recurrence is felt acutely by the patient who does not wish to disappoint the health care team by inadvertently stumbling onto territory that questions positive treatment outcomes.

Though it is understandable and to some degree acceptable as a normal reaction to having been treated for cancer it is important to gain an awareness from patients about the level of FOR that they commonly experience. This is highlighted in research evidence that strongly suggests that, in some patients, FOR is associated with substantial psychological morbidity [7,9]. In the breast cancer PCI those patients expressing more than three fears had significant distress. In those patients with H&N cancer raising the issue of FOR on the PCI, 79% had significant problems compared to 24% if they did not [7]. The current understanding of FoR levels across various cancer sites shows a strong similarity of intensity. However prostate cancer patients tend to have lower levels of FoR compared to breast, lung and colorectal cancer patients. The greatest functional impact of FoR was found in lung cancer patients. Some patients with high levels of FoR show some characteristics of thoughts becoming intrusive and uncomfortable [10]. This type of thinking showed evidence of not being able to dismiss the content about the possibility of the cancer returning. This intrusive thinking was regarded as an area requiring some specific attention from trained personnel to assist patients.

The mechanism of how high levels of FOR may be linked to distress and, in particular, to depression is not well understood. The associations are relatively high and theoretically various convincing psychological models can be proposed that would explicate a causal connection [11]. The manifestations of enhanced FOR are expressed by excessive checking, over-vigilance, intrusive FOR thoughts frequently during the day, poor sleep, and anxiety. There is likely to be a hidden cost to persistent FOR. Not only poorer quality of life [12], delayed adaptation (time off work), but also more frequent hospital attendances, and unnecessary investigations [13]. Once identified the provision of key information during the consultation is often all that is required. Information giving around risk, normalising the experience of FOR, empathy and basic counselling will be sufficient for the majority of patients (Table 1). Patient information leaflets are available focused on the issue of FOR [14]. Although there are several useful websites (Table 2) there is still probably a need for refinement in order to have a resource that more fully meets the needs of patients. From clinical experience, various survey and qualitative investigations show that some patients, perhaps around 20%, have sufficient difficulties associated with FOR that they would need formal referral for emotional support or cognitive therapy to be delivered by staff with a special interest in emotional issues, counselling staff or clinical psychologists. Although various therapies will have potential generic benefit such cognitive behavioural therapy or mindfullness-

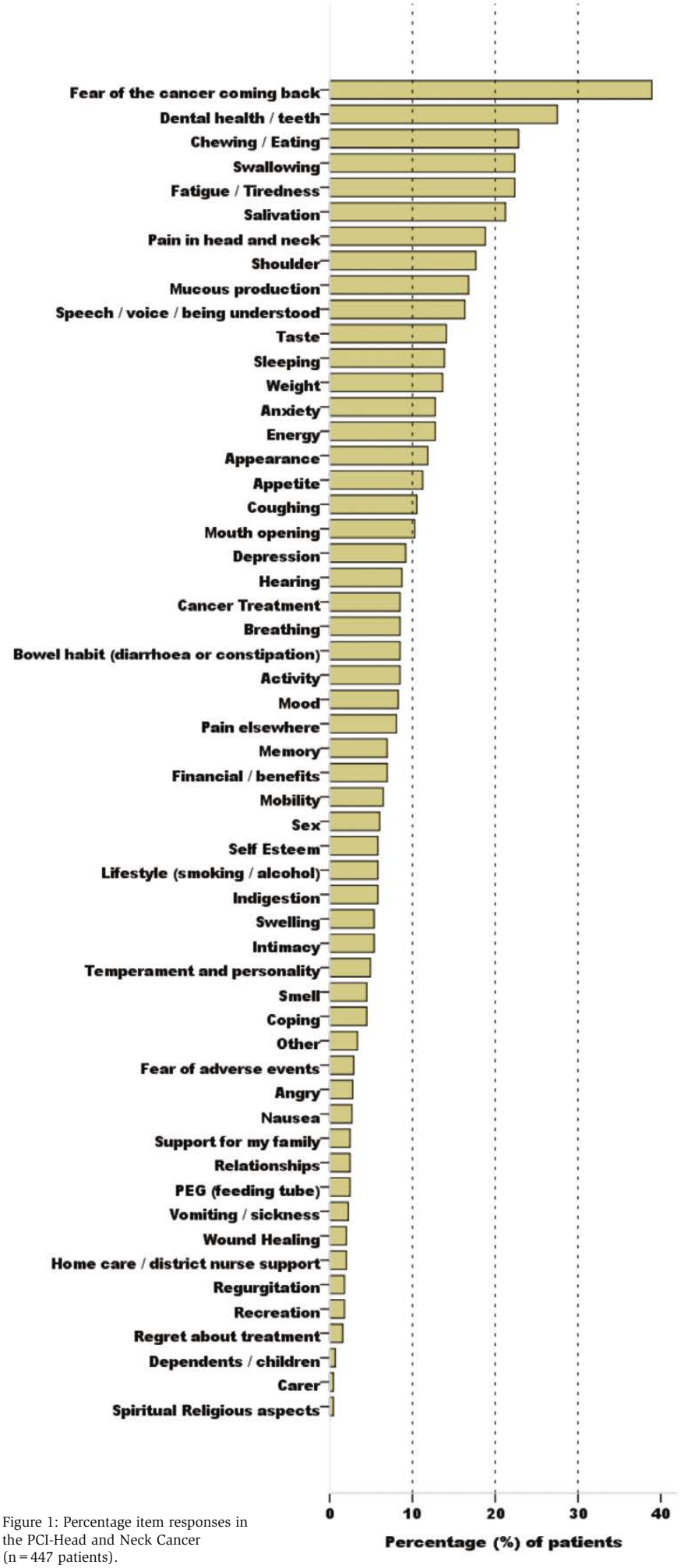

Figure 1: Percentage item responses in the PCI-Head and Neck Cancer (n = 447 patients).

based interventions, there is some evidence that suggests more specific intervention around recurrence fears would be appropriate [11]. Such an intervention is the AFTER intervention, Adjustment to the Fear, Threat or Expectation of Recurrence [15]. This structured intervention targets recurrence fears, inappropriate checking behaviour, and beliefs about cancer, adopting recognised cognitive behavioural and health psychology principles, particularly Leventhal's self-regulation model. The intervention focuses on reducing anxiety (through exposure to the fear of recurrence) and purports to prevent long term psychological distress and promote patients ability to self manage.

The AFTER intervention can be framed within the context of busy NHS practice through the delivery of a mini AFTER delivered in part by individuals with counselling training and advanced communication skills. The mini AFTER is being designed for a trained staff member of the oncology team to conduct in a single session lasting about 30 minutes. It aims to assess the FOR level and determine the triggers of FOR and how the patient currently attempts to manage the fear. At moderate levels this very brief intervention will perform three functions: (i) signal to the patient that their fears are reasonable and can be understood (ii) identify the main components that have raised these fears and present some possible explanations for their intrusiveness and inability to cope with them, finally (iii) provide patients and any accompanying carers the opportunity to discuss potential ways to address these fears in a practical and easy to follow manner. It is reasonable to target the intervention for both the patient and the carer. Carers have been shown to exhibit FOR, and on average show levels that are as high if not higher than the persons they are supporting who are being treated for cancer. Some evidence exists that there is a close association between carers and patients FOR [16]. This work has led some investigators to state that the management of concerns about cancer coming back' is one of the top ranking unmet needs across time included amongst carers [17].

Patients with more extensive and deeper seated FOR may require a more elaborated input from the team. The more intensive AFTER intervention consisting typically of six sessions can be offered. This intervention is being developed from the initial

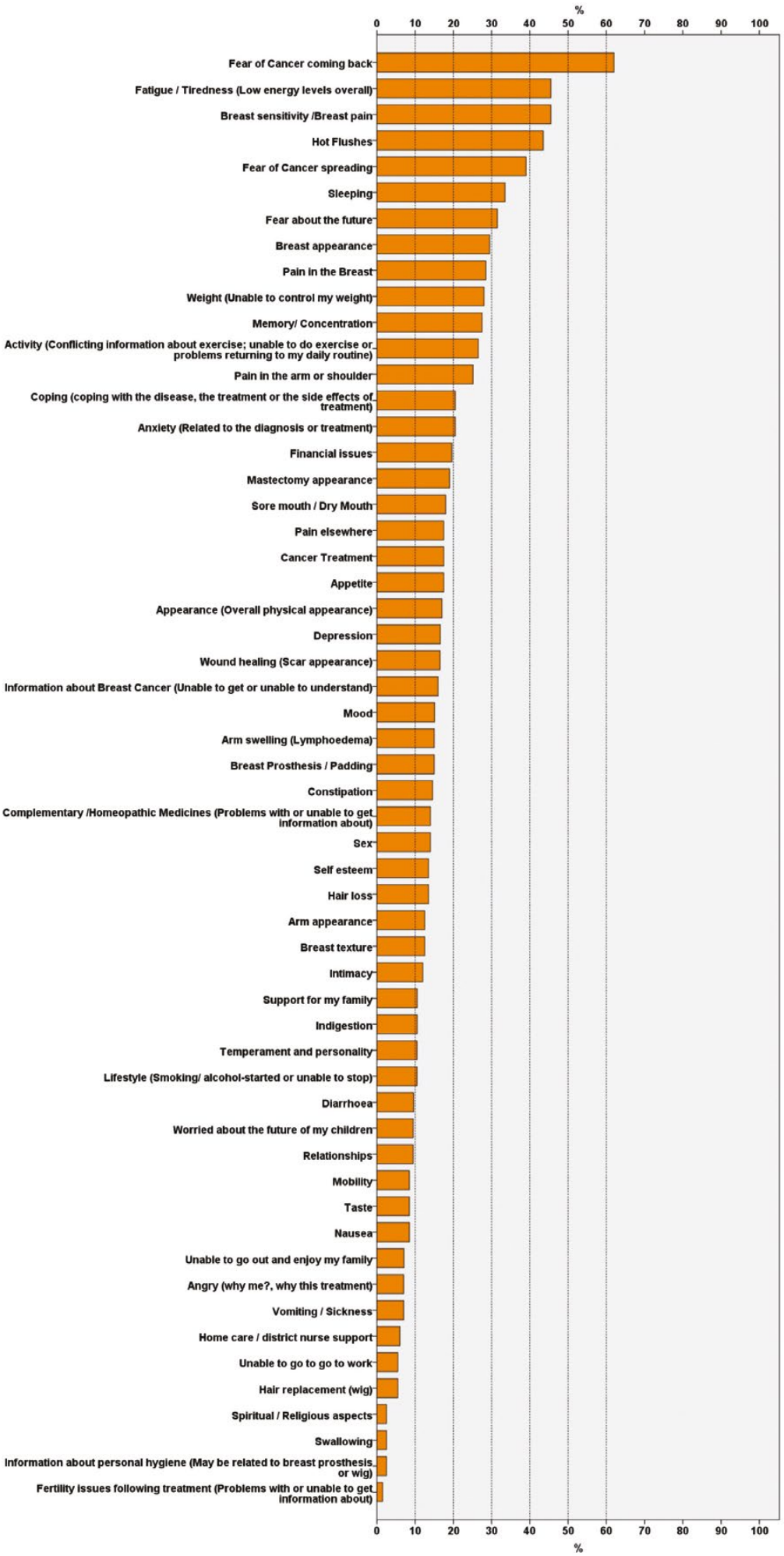

Figure 2: Percentage item responses in the PCI-Breast Cancer (n = 200 patients)

research work by Humphris and colleagues, first at Liverpool and more recently at St Andrews/Edinburgh and NHS Fife. It is intended that the intervention will be available shortly through web access under a registered low cost licence scheme for interested professionals. The elements of the intervention are listed in Box 1 below. More research is required as to how to most cost effectively deliver such intervention and this lends itself to a well designed randomised trial. ■

Box 1: Outline of AFTER intervention.

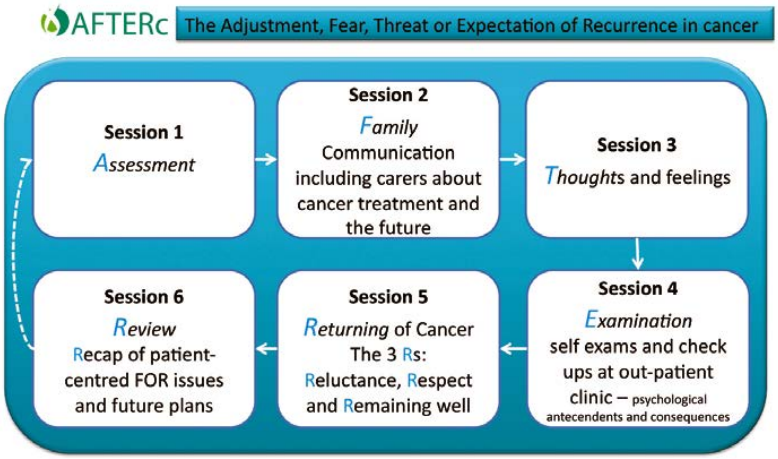

Table 1: Points around advice on fear of recurrence.

Patients should be confident to raise the issue with their cancer team as it is such a common issue. Although it can be a taboo subject but it is better to discuss it.
Questions patients might wish to ask at any stage during their cancer care but usually after treatment has been completed and acute side effects are fading and a 'new normal' is immerging. Patients need to be reassured that FOR is normal and potentially a positive feeling as it promotes self checking.
Information around recurrence should be tailored to the cancer site.
The clinical team should be able to cover aspects such as: 1. what are the chances of the cancer coming back 2. when is the cancer most likely to come back 3. where is it most likely to come back to 4. what are the symptoms and the things to look out for 5. do investigations such as scans or blood tests give more certainty that recurrence is less likely 6. what can be done if it comes back 7. what is the outlook (chance of cure) 8. when can their be confidence that there is cure (e.g 5 years, 10 years, never) 9. who do I contact if the patient think the cancer is coming back- contact the clinic, consultant secretary, CNS, open access 10. what guide is there to self help e.g discussion around patient information leaflets material available in clinic 11. let others know, the wider team and the GP 12. can I get specialist support e.g AFTER intervention

Table 2: Useful websites.

http://cancer.about.com/od/copingwithcancer/f/How-So-I-Cope-With-The-Fear-Of-Cancer-Recurrence.htm
http://cancer.about.com/od/copingwithcancer/f/How-So-I-Cope-With-The-Fear-Of-Cancer-Recurrence.htm
http://www.cancer.net/coping/emotional-and-physical-matters/coping-fear-recurrence
http://www.cancer.org/treatment/survivorshipduringandafttertreatment/understandingrecurrence/livingwithuncertainty/living-with-uncertainty-toc
http://www.dana-farber.org/For-Adult-Cancer-Survivors/Experts-Speak-on-Survivorship-Topics/Fear-of-Cancer-Recurrence.aspx
http://www.headandneckcancer.co.uk/For+patients/Problems+and+Solutions/Fear+of+Recurrence.aspx
http://www.livestrong.org/Get-Help/Learn-About-Cancer/Cancer-Support-Topics/Emotional-Effects-of-Cancer/Fear-of-Recurrence
http://www.mayoclinic.com/health/cancer-recurrence/MY01877
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Awards & Appointments

2013 ESMO Award

Professor Cora Sternberg from San Camillo Fortanini Hospital, Rome, Italy won this award. She is an internationally respected leader in the field of urological malignancies: she has been elected Board Member of the European Organisation for Research and Treatment of Cancer (EORTC) for three terms; ESMO Faculty Coordinator for Genitourinary Tumours for many years and also served on the ESMO Nominating Committee, which is responsible for identifying candidates for ESMO high-level posts. Prof Sternberg is currently the Solid Tumor editor of Critical Reviews in Oncology and Hematology and the Genitourinary Cancer editor for the European Journal of Cancer. She is the ESMO Scientific Co-Chair of this year's ECC Congress.

Best known for her seminal work in bladder cancer, research on targeted agents in renal cell carcinoma and novel therapies for prostate cancer, Prof Sternberg is Chief of the Department of Medical Oncology at the San Camillo Forlanini Hospital and Adjunct Professor at La Sapienza University, Rome, Italy. Honours bestowed upon her in Italy include the title 'Grande Ufficiale al Merito della Repubblica Italiana' and the Premio Minerva for Scientific Achievement, XVIII Edition for Achievements in Science. ■

2013 ESMO Lifetime Achievement Award

Franco Cavalli won this award, he is from the Instituto Oncologia Svizzera Italiana, Bellinzona, Switzerland. Prof Cavalli was formerly Chair of the Swiss Group for Clinical Cancer Research and was president of the Swiss League against Cancer during 2001-2004. He is currently Chair of the Scientific Committee of the European School of Oncology (ESO) and from 2006 to 2008 was President of the International Union Against Cancer. Prof Cavalli has authored or co-authored more than 550 scientific articles and five books including the 'Textbook of Medical Oncology'. Among his collection of international awards are the Pezcoller Award, the New Drug Development Organisation Honorary Award, the Greidinger Award (Israel) and the Waldman Award (USA).

Prof Cavalli's research began in leukaemia and he represented Switzerland in the Cancer and Leukaemia Group B (1975-1985). He later worked on breast cancer and now studies malignant lymphomas. He was instrumental in creating the International Extranodal Lymphoma Study Group. Every second year he organises the International Conference on Malignant Lymphoma in Lugano, the leading international forum for basic and clinical research in lymphomas. ■

2013 Hamilton Fairley Award

This was awarded to Roger Stupp of the Universitätsspital Zurich, Switzerland. Prof Stupp is known worldwide for his research on malignant gliomas, head and neck as well as lung cancers. He has been the lead investigator for establishing the use of temozolomide chemotherapy in conjunction with radiotherapy in newly diagnosed glioblastoma and determining the predictive value of MGMT gene-promoter methylation. His special clinical interests include new drug development and the association of chemotherapy and radiation. His work in clinical research has contributed to an important practice change in the neurooncology filed, introducing novel chemotherapeutics after many years.

He is Professor at the University of Zurich, Switzerland, Chair and Director of the Department of Oncology of the University Hospital Zurich and the Zurich Cancer Centre. Prof Stupp maintains close collaborations with Prof Monika Hegi, head of the Laboratory of Tumour Biology and Genetics at the CHUV in Lausanne, the Laboratory of Tumour Angiogenesis and Microenvironment led by Prof.Curzio Ruegg, and the Swiss Institute of Experimental Cancer Research (ISREC). ■

World-renowned cancer scientist lands top job

Professor Patrick Johnston, Dean of the School of Medicine, Dentistry and Biomedical Sciences at Queen's has been announced as the University's 12th President and Vice-Chancellor and will take up post early in 2014.

Speaking about his appointment, Professor Johnston said: "This is a proud day for both me and my family and I thank Queen's University for choosing me to be its next President and Vice-Chancellor. I very much look forward to leading this distinguished institution and working alongside its exceptional staff and students."

A globally-recognised cancer specialist, Professor Johnston, born in 1958, has always been a high achiever. A past pupil of St Columb's College, Derry, he received his MB BCh degree in Medicine with distinction from University College Dublin in 1982. In 1987 he obtained a Fellowship at the National Cancer Institute (NCI), USA, where he began further clinical training in Medical Oncology. He was promoted to senior investigator status at NCI in 1991. ■

Journal Reviews

Clinical Breast Cancer

Intraductal breast Papilloma diagnosis and treatment with vacuum-assisted core biopsy

Vacuum-assisted core biopsy in diagnosis and treatment of intraductal papillomas
Kibil W, Hodorowicz-Zaniewska D, Popiela TJ, Kulig J.
Clinical Breast Cancer 2013;Apr;13(2):129-32.

The aim of this study was to assess the value of mammographically-guided and ultrasonographically-guided vacuum-assisted core biopsy (VACB) in the diagnosis and treatment of intraductal papillomas of breast and to answer the question whether ductal biopsy by this method allows the avoidance of surgery in these patients. The study is based on the findings from a 10 year period (2000-2010) during which a total of 1896 vacuum-assisted core biopsies were performed. Of these, 1183 biopsies were performed ultrasonographically guided and 713 mammographically guided (stereotaxic). Only 62 patients (3.2%) histopathologic examination confirmed intraductal papilloma of which 12 patients (19.4%) had atypical lesions at the initial examination. An open surgical biopsy of these 12 patients revealed invasive cancer in 2 women (false-negative rate, 16.7%; negative predictive value, 83.3%) and the biopsy from the remaining 50 patients (80.6%) revealed papilloma without atypia. All the 50 patients were later followed up to average of 5 years (range 14 months-10 years) by clinical observation and imaging examinations and did not show recurrence or malignant transformation of lesions. Hematoma developed in 3 (4.8%) patients as a complication of biopsy and surgical intervention was not required in any of the patients. In conclusion, authors' states that VACB is an efficient method for diagnosing intraductal papilloma of the breast and allows histopathologic confirmation of the lesion. Benign lesions corresponding to the clinical presentation can be managed conservatively avoiding surgery. However in all cases, histopathologic diagnosis of papilloma with atypical hyperplasia or a suspected malignant lesion on imaging, despite negative biopsy results, should always be an indication for surgical excision.

Reviewer's opinion: This study looked at the usefulness of VACB (US and Mammo guided) for the diagnosis and treatment of intraductal breast papilloma. The study even though aims to present 10 year data from a large pool of study population, however, the actual true positives were only 62 patients (3.2%) out of 1896 VACB performed. The low sample number may be in keeping with the uncommon prevalence of benign neoplasm that occurs in 2 to 3% of the population. The authors argue a case for conservative management for benign neoplasms on histology with annual surveillance with clinical, US and mammographic examinations up to 5 years without being explicit in their data as to how many image diagnosed benign lesions were completely removed with VACB. If VACB is a good technique to completely remove the lesion, why are the authors recommending an open excision biopsy for papillomas with atypical features. Alternatively, if the authors mean that VACB can help provide a diagnosis facilitating a definitive treatment later with open excision biopsy, the word 'treatment' in the context of VACB has been used interchangeably. The opinion on conservative management of papillomas without atypia seems to divided as other studies have found a higher risk of malignancy in this group. – TH

Neuro-Oncology

IDH/*MGMT*-driven molecular classification of low-grade glioma is a strong predictor for long-term survival

Leu S, von Felten S, Frank S, Vassella E, Vajtai I, Taylor E, Schulz M, Hutter G, Hench J, Schucht P, Boulay JL, Mariani L. Neuro-Oncology 2013;15(4):469-79.

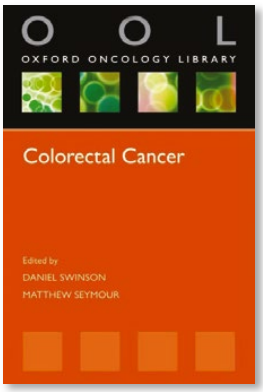
Compared with the most malignant subtype of brain tumour, i.e. glioblastoma multiforme (GBM; grade IV), low-grade gliomas (LGGs; grade II) are rare and the median survival times span up to a few decades. LGGs progress in an infiltrative manner and develop into malignant tumours (grades III and IV). Grade IV tumours deriving from LGGs are designated secondary GBM and represent a small subset of GBM (~5%), compared with the more frequent primary GBM (~95%), which are considered to have developed *de novo*. Two molecular alterations characteristic of glioma have a particularly high prevalence in LGG: *MGMT* gene promoter methylation (*MGMT*met) and *IDH1*/*IDH2* mutations (*IDH*mut). Previous studies found that 41% of gliomas carried an *IDH1* mutation, whereas 2% had an *IDH2* mutation in a mutually exclusive manner. *IDH1/2* gene mutations were mostly observed in LGGs (70%–80%) and in secondary GBM (85%), compared with primary GBM (3%–7%). *TP53* mutations (*TP53*mut) mainly occur in diffuse astrocytomas, and are also associated with a younger age of onset and a shorter survival. Combined loss of heterozygosity of 1p/19q (1p19qLOH) is prevalent in oligodendrogliomas and is an indicator of longer survival. In this study, 210 adult LGGs were screened for *IDH*mut, *MGMT*met, 1p19qLOH, and nuclear *TP53* immunopositivity (*TP53*pos). Multivariate survival analyses with multiple imputation of missing data were performed in order to evaluate the impact of those biomarkers on survival. The results showed that molecular parameters were better survival predictors than histology ($P<.001$). *MGMT*met was positively associated with *IDH*mut ($P<.001$). IDHmut/MGMTmet combined status had a favourable impact on overall survival whereas *IDH*mut/*MGMT*met/*TP53*pos triple combination was a significant risk factor for malignant transformation ($P<.05$). The present study suggests that genotype better predicts prognosis than histology and therefore provides a more reliable tool for standardising future treatment strategies.

Reviewer's opinion: The impact of *IDH1*/*IDH2* mutations on survival among patients with LGG has been disputable with some studies showing no impact while others suggesting a positive correlation between *IDH* mutations and overall survival (OS). Results from this detailed retrospective study show that *IDH*mut, in combination with *MGMT*met, has a significant positive impact on long-term OS. Furthermore, a combination of biomarkers investigated in this study, along with demographic and clinical variables, provides a stronger survival predictor for LGGs than histological analysis alone. Based on their data, the authors made a statement that such markers should be routinely assessed in parallel to histopathological examination to better predict prognosis for patients with LGG. Their findings could also help standardise therapeutic strategies and identify novel targets for future therapies. – QA

Book Reviews

Oxford Oncology Library – Colorectal Cancer

Editors: Daniel Swinson, Matthew Seymour. Published by Oxford University Press. ISBN: 978-0-19-959020-9. Price: £19.99.



This is a valuable book of 124 pages covering a summary of comprehensive information regarding colorectal cancer. This book is useful for final year medical students and for foundation doctors. It is also a refresher for MRCS part A in colorectal cases and for researchers with interest in colorectal surgery. It contains 12 chapters.

Chapter one deals with the introduction, aetiology, staging, histology and epidemiology of the colorectal cancer. In particular it focuses on modifiable and unmodifiable risk factors, highlighting genetic factors and their associated syndromes.

Chapter two is dealing with the clinical presentation of colorectal cancer and also deals with screening and different varieties of investigations. Finally it demonstrates a new novel technique with proteomics that entails protein analysis from easily accessible body fluids such as blood and urine.

Chapter three is dealing with the surgical options for the management of colorectal cancer and the indication of each option and in chapter four we can read details on the role of radiotherapy in colorectal cancer. It also includes details on treating local advanced disease to achieve curative resection.

Chapters five to seven are focusing on the pharmacology of anti-cancer drugs used in colorectal cancer with the mechanism of action. All the side effects of Flurouracil (5-FU), Capecitabine, Oxaliplatin, & Itinotecan, are mentioned.

Chapter eight is dealing with the type of surgery for recurrent rectal and colonic cancer, depending on its location and also the contraindications to this surgery.

In Chapters nine and ten we can read details on different surgical procedures used in liver and pulmonary metastasis and their techniques depending on the patient selection.

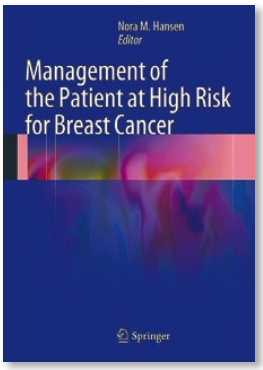
Chapter eleven is dealing with surgical and non-surgical palliation of colorectal cancer with the importance of presence of multidisciplinary team. Palliative approaches for inoperable bowel obstruction treating symptoms of bowel obstruction are all covered, in addition to the symptoms of tenesmus, rectal bleeding and mucous discharge.

The last chapter discusses the new therapeutic avenues in colorectal cancer in terms of immunotherapy such as vaccines and their related researches. Examples of other therapeutic approaches are organ directed therapy, liver radiotherapy, local ablative techniques, hepatic arterial radioembolization and selective internal radiotherapy brachytherapy with Ytrium-90. ■

Dr Ahmad Nabil Al-Chalaby,
MBChB, AFHEA, Foundation Year 2 trainee, West Midlands Deanery, UK.

Management of the Patient at High Risk for Breast Cancer

Editors: Nora M. Hansen. Published by: Springer. ISBN: 978-1-4614-5890-6. ePrice: £100.50 Hardback £126.00



This book has in total has 181 pages and is divided into 13 chapters. Each chapter is written by a different author and overall the book covers a range of topics from the genetic and genetic factors in breast cancer to the current and future directions in breast translational research.

The first chapter of the book titled "Identifying Women at High Risk of Breast Cancer: Understanding the risk models" sets the scene perfectly for the readers as it sketches in detail the most commonly used empiric and genetic risk prediction models, summarising the pros and cons of each model. This chapter helped improve my understanding of the IBIS (Tyrer-Cuzick) model that I routinely use in my clinical practice.

The second chapter of the book discuss the genetics and genetic factors in breast cancer, covering various genetic syndromes and the high risk genes that are responsible for early onset breast cancer. Also, a section is dedicated to quantitative and qualitative cancer risk assessments and discusses a few risk assessment models. Further, chapter three details a brief but targeted discussion on BRCA mutations and their role in breast cancer along with surveillance and management strategies for BRCA carriers.

Chapters four to eight mainly focus on the management aspects of the patients at high risk of breast cancer. Personally, I liked reading chapter seven and eight which mainly focus on the medical and surgical risk reduction management strategies.

Chapter nine focusses on the advance breast reconstruction options and the schematic representations and the breast reconstruction pictures are of high quality and aid in understanding the textual content very well. Chapter ten discusses the management of concomitant risk-developing other malignancies in individuals with a genetic predisposition to breast cancer. I found this chapter an add-on to the main topic and mainly highlighted the management protocols of other associated cancers. Chapters eleven and twelve focus on psychological implications of testing positive for BRCA gene and the high-tech high risk clinics. The last chapter mainly highlights the current and future state of translation research on breast cancer, preventive vaccines and major challenges in non-invasive monitoring of pre-cancerous disease progression.

Overall, I have found this to be a very well illustrated text, easy to read and very informative. I would definitely recommend this book as a good read to both surgeons and oncologists. ■

Tasadooq Hussain BA (Edu.) MD MRCS;
Clinical Research Fellow Breast Surgery; Cancer Biology Proteomics Group, University of Hull-HYMS; Hull and East Yorkshire Hospitals NHS Trust; Hull; UK.

Conference Digest

Reports from the European Cancer Congress (ECCO-ESMO-ESTRO)

Date: 27 September - 1 October 2013; Amsterdam, The Netherlands.

Cetuximab improves overall survival in RAS-wild type mCRC

Treatment with cetuximab plus FOLFIRI is associated with a median increase in overall survival of 7.5 months in patients with metastatic colorectal cancer (mCRC) with RAS wild-type tumours compared to treatment with bevacizumab, according to new data from a pre-planned analysis of the FIRE-3 study reported during a late-breaking session at the congress.

The independently led study included 752 patients with mCRC; 592 of these had confirmed KRAS exon 2 wild-type tumours and were randomised to treatment with cetuximab plus FOLFIRI or to bevacizumab plus FOLFIRI. Further analysis of the 407 patients with samples available for further RAS mutation analysis revealed that 84% had RAS wild-type tumours and 16% had RAS mutant tumours other than KRAS exon 2.

Results showed that median overall survival was 33.1 months in mCRC patients with RAS wild type tumours given first-line treatment with cetuximab plus FOLFIRI compared to 25.6 months in those randomised to bevacizumab plus FOLFIRI (hazard ratio 0.70, 95% confidence interval 0.53-0.92, p = 0.011). The overall response rate was higher with cetuximab (65.5%) than with bevacizumab (59.6%).


Prof Volker Heinemann

"The most important endpoint – overall survival – showed a significant 7.5 month increase with first-line cetuximab plus FOLFIRI compared to bevacizumab plus FOLFIRI," said lead investigator Professor Volker Heinemann, from the Ludwig-Maximilians University, Munich, Germany. He added, "Such a prolongation is a paradigm shift in mCRC treatment since the introduction of monoclonal antibodies." He considered that, taken together with findings from other studies, the results suggest that first-line treatment of RAS wild-type patients should include an anti-EGFR therapy. ■

Susan Mayor PhD, Medical Journalist.

Study shows 'irrefutable' evidence that colorectal cancer screening reduces deaths

Screening for colorectal cancer (CRC) achieves major reductions in deaths from the disease, shows a major review of data from European countries.

Professor Philippe Autier, Vice-President, Population Studies at the International Prevention Research Institute, Lyon, France reported results from data collected as part of the Survey of Health, Ageing and Retirement in Europe (SHARE) project on the impact of screening in men and women aged 50 and over in 11 European countries between 1989 and 2010. His research group used the World Health Organization database on cause of death to calculate changes in death from colorectal cancer in different countries, relating these to CRC screening activities.

"We saw quite clearly that the greater proportions of men and women who were screened, the greater the reductions in mortality," Professor Autier told the congress. "Reduced death rates from CRC were not seen in countries where screening was low even though healthcare in those countries was similar to countries where screening was more widespread."

Deaths from CRC fell by 39% in men and 47% in women in Austria, where 61% of people included in the survey had undertaken a faecal occult blood test during the study period. In contrast, CRC deaths increased by 30% in men and 2% in women over the same time, where only 8% of males had an endoscopic examination compared to 35% in Austria.

Overall, 73% of the decrease in CRC mortality in males and 82% in females could be explained by their having undergone one or more endoscopic examinations of the large bowel over the last ten years. "The evidence could not be clearer. CRC screening reduces mortality and probably also CRC incidence and is as effective in prevention as cervical screening," concluded Professor Autier. "It is therefore very disappointing that national differences in the availability of CRC screening programmes are still so pronounced." ■

Susan Mayor PhD, Medical Journalist.

Cancer survival is associated with government health care spending

The more a government spends on health, the fewer deaths from cancer, according to a major study across 27 EU countries.

Researchers at the Breast European Adjuvant Studies Team, Belgium, analysed information on populations, cancer incidence and mortality from the World Health Organization at the same time as health care spending based on information from the International Monetary Fund and the World Bank. They compared wealth and health expenditure indicators with estimates of the proportion of patients dying after a cancer diagnosis.

Around 60% of patients died after a diagnosis of cancer in countries spending less than 2000 US dollars per capita on health care per year, including Romania, Poland and Hungary. This fell to 40-50% of patients dying in countries spending 2500-3500 US dollars in countries such as Portugal, Spain and the UK. Fewer than 40% of patients died in countries spending around 4000 US dollars per year, including France, Belgium and Germany.

The difference in death rates was even marked when the group analysed data for breast cancer, as an example of a cancer with effective screening methods.

"Our research demonstrates that despite initiatives to make healthy policy more uniform across EU member states there are still marked differences between Eastern and Western Europe in regards to cancer indicators," said lead investigator Dr Felipe Ades, a medical oncologist from the study team. "We conclude that the more a country spends on health, the lower the risk of death after a cancer diagnosis. This is particularly the case for cancers with effective screening and treatment options, such as breast cancer." ■

Susan Mayor PhD, Medical Journalist.

PV-10 continues to show robust effect in cutaneous Stage III-IV melanoma

Injecting cutaneous lesions in Stage III-IV melanoma patients refractory to other treatments with PV-10 provides a viable strategy to maintain long-term locoregional control, concluded the final analysis of an open label phase 2 trial. The study, presented at ECC2013, found both the number of lesions injected and presence of blistering to be prognostic for outcome.

"Our take home message is that if you inject cutaneous lesions with PV10 there's a one in two chance that you'll achieve a clinical response, and an additional one in two chance of a non injected lesion responding," said study presenter Dr Sanjiv Agarwala, from St Luke's Hospital, Bethlehem, Pennsylvania. Such results, he added, were remarkable in a patient population refractory to a median of six previous interventions, over half of whom were aged over 70 years.

PV-10, a 10% solution of Rose Bengal, has been developed to selectively target and destroy cancer cells without harming surrounding healthy tissue, minimizing the potential for systemic side effects.

In the open label single arm trial, 80 patients with stage III-IV melanoma received up to four courses of PV-10 injected in up to 20 cutaneous or subcutaneous lesions on the extremities and, or torso. Furthermore, up to two bystander lesions with confirmed melanoma that did not receive treatment. The primary endpoint was best overall response rate (BORR) judged by modified RECIST (mRECIST) in each subject's target lesions.

Results showed that for all subjects, BORR was 51% (26% complete response, 25% partial response) with the amount of tumour burden accessible to PV-10 injections prognostic for outcome. Subjects who had uninjected bystander lesions achieved a BORR of 54%, while subjects who had all their lesions injected achieved a BORR of 71%.

Locoregional blistering, which generally occurred within seven days of PV-10 injection and typically resolved within four weeks, affected 40% of subjects. BORR was 66 % for subjects with blisters versus 42 % for those without.

"If blistering occurs you can reassure patients they're likely to achieve a good response. It provides further evidence for an immunological basis for the mechanism of action," said Dr Agarwala.

Based on the immune mechanism of action, he added, PV-10 was likely to work well in combination with other immunotherapies, such as ipilimumab. Provectus Pharmaceuticals, Inc, (Knoxville, Tennessee, USA), the company developing PV-10, believes they now have sufficient information to seek regulatory approval. ■

Janet Fricker, Medical Journalist.

Cediranib increases survival in recurrent ovarian cancer

Cediranib plus chemotherapy significantly increased survival in patients with recurrent ovarian cancer, reported the phase III ICON6 study at the ECC2013 meeting.

Cediranib, which is taken orally, is a tyrosine kinase inhibitor which blocks VEGF receptors controlling the development of blood vessels required for tumour growth. "This is the first trial to demonstrate a significant improvement in the progression-free and overall survival with an oral VEGF tyrosine kinase inhibitor in ovarian cancer, and these results suggest that cediranib has a clinically meaningful role in the treatment of recurrent ovarian cancer," said Professor Jonathan Ledermann, the study presenter from the University College London(UCL) Cancer Institute.

In the three arm study 456 patients with relapsed platinum-sensitive ovarian cancer were randomized to receive 20 mg a day of cediranib during chemotherapy followed by placebo for 18 months (concurrent arm of the trial); or 20 mg a day of cediranib during chemotherapy followed by cediranib as maintenance treatment (maintenance arm); or to receive platinum based chemotherapy together with a placebo (reference arm). Patients were enrolled from 63 centres in the UK, Canada, Australasia and Spain, with the primary analysis comparing the maintenance and reference arms.

Results show that median progression free survival (PFS) was 11.1 months in the cediranib maintenance arm versus 8.7 months in the chemotherapy arm (HR 0.57; P = .00001). Due to non proportional hazards in the two treatment groups, Ledermann and colleagues went on to perform a restricted means analysis, which resulted in a median PFS of 12.5 months in the maintenance arm versus 9.4 months in the reference arm.

Median overall survival was 26.3 months for the cediranib maintenance arm versus 20.3 months for the chemotherapy arm (HR 0.70; P = 0.042). The most common adverse events were hypertension, fatigue, diarrhoea, and nausea, which could be controlled with dose reductions or interruptions.

Despite such favourable results the future of cediranib in ovarian cancer remains uncertain since the manufacturer AstraZenica ceased its development in September 2011 following disappointing results in first-line metastatic colorectal cancer and non-small cell lung cancer. ■

Janet Fricker, Medical Journalist.

Combination approach shows promise in glioblastoma

Combining radiotherapy with a new fusion protein anti-cancer drug APG101 improved survival for patients with recurrent glioblastoma, reported a phase 2 study at the ECC2013 meeting.

APG101 is a fusion protein similar to an antibody that blocks the CD95 cell-signalling pathway that plays a crucial role in enabling migration and invasiveness of cancer cells. The molecule was designed to inhibit interaction between the CD95 ligand and CD95 receptor. "It was already known that APG101 might be an innovative approach for treating glioblastoma, but the size of the protein molecule was potentially too large to cross the protective blood-brain barrier and target the tumour. Radiotherapy opens up this barrier and may therefore be an effective vehicle for this compound," said study presenter Wolfgang Wick from the German Cancer Research Centre at the University of Heidelberg. The study, he added, was the first controlled trial of re-irradiation.

In the study 84 glioblastoma patients who had already received initial treatments including radiotherapy and showed cancer recurrence, were randomized to receive either radiotherapy (RT)alone or RT together with an intravenous dose of 400 mg APG101 once a week. The trial was carried out between December 2009 and September 2011 in 25 centres in Germany, Austria and Russia.

Results showed that six months after treatment 21% of patients treated with the combination of RT and APG101 were alive compared to 4% of those treated with radiotherapy alone. Median overall survival (OS) was 11.5 months in the RT arm versus 11.8 months in the APG101 arm.

A subgroup analysis of patients with CD95L positive tumours showed that median overall survival was 8.2 months in the RT arm versus 11.5 months in the APG101 arm. But for patients with CD95L negative tumours median overall survival was 15 months in the RT arm versus 13.5 months in the APG101 arm.

"This implies that CD95L would be one of the first predictive markers in neuro-oncology, which may help to define patients with glioblastoma deriving benefit from the new therapeutic strategy. At present there is paucity of predictive markers that tell us how to treat patients in the glioma field," said Professor Wick. ■

Janet Fricker, Medical Journalist.

Diary of Events

To have your event listed in the Oncology News diary e: Patricia@oncologynews.biz by December 10th 2013.

November

NEW
6th Royal Marsden Pain and Opioid Conference
1 November 2013; London, UK
W: www.royalmarsden.nhs.uk/painconference
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

NEW
Gynaecological Cancers Study Day
6 November 2013; London, UK
W: www.royalmarsden.nhs.uk/gynaestudy
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

Supportive & palliative care for cancer patients
5 November 2013; Middlesex, UK
E: anni.hall@nhs.net

PRiMa Conference: Pain and Symptom Management in Supportive and Palliative Care
7 November 2013; Manchester, UK
W: www.christie.nhs.uk/school-of-oncology/education-events
T: +44 (0)161 446 3773
E: education.events@christie.nhs.uk

Essential Communications Skills
7 November 2013; Middlesex, UK
E: anni.hall@nhs.net

Thoracic Imaging - Hot Topics 2013
8 November 2013; London, UK
W: www.rcr.ac.uk

Biological Basis of Cancer Therapy – Pharmacology, Chemotherapy, Molecular Biology
11-15 November 2013; Manchester, UK
W: www.christie.nhs.uk/school-of-oncology/education-events
T: +44 (0)161 446 3773
E: education.events@christie.nhs.uk

NEW
17th Russian Oncological Congress
12-14 November 2013; Moscow, Russia
E: congress@russco.org
W: www.ronc.ru

Practical Developments in Skin Cancer Treatment: Brachytherapy & PDT
14 November 2013; Manchester, UK
W: www.christie.nhs.uk/school-of-oncology/education-events,
T: +44 (0)161 446 3773 or
E: education.events@christie.nhs.uk

NEW
5th Annual Royal Marsden Head and Neck Conference
15 November 2013; London, UK
W: www.royalmarsden.nhs.uk/headneckconference

Breast Cancer Care Annual Conference 2013
15 November 2013; London, UK
E: nursingnetwork@breastcancercare.org.uk
W: www.breastcancercare.org.uk/annualconference
#BCCAnnualConference

NEW
UK Breast Cancer Meeting (UKBCM)
15-16 November 2013; London, UK
Janis Troup
T: +44 (0)7885 020828
E: info@rightangleuk.com
W: www.ukbcm.org.uk

NEW
Advances in the Diagnosis and Treatment of Lung Cancer
21 November 2013; London, UK
W: www.royalmarsden.nhs.uk/lungadvances

1st Indian Cancer Congress
21-24 November 2013; Delhi, India
W: http://indiancancercongress2013.org

NEW
Royal Marsden Haemato-Oncology Study Day
25 November 2013; London, UK
W: www.royalmarsden.nhs.uk/haematooncology
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

NEW
Advances in the Nutritional Care of Cancer Patients
26 November 2013; London, UK
W: www.royalmarsden.nhs.uk/nutritionalcare
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

NEW
Transfusion Awareness
26 November 2013; Manchester, UK
www.christie.nhs.uk/school-of-oncology/education-events
T: +44 (0)161 446 3773
E: education.events@christie.nhs.uk

Rehabilitation in Cancer Care
28-29 November 2013; Manchester, UK
www.christie.nhs.uk/school-of-oncology/education-events
T: +44 (0)161 446 3773
E: education.events@christie.nhs.uk

December

NEW
Molecular Mechanisms of Targeted Cancer Treatments
5 December 2013; London, UK
W: www.royalmarsden.nhs.uk/molecular
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

Controversies in The Management of Head & Neck and Thyroid Cancer
5-6 December 2013; London, UK
E: gemma.jones@inhanse.org

Cardiology & Cancer in Primary Care
9 December 2013; Manchester, UK
W: www.christie.nhs.uk/school-of-oncology/education-events
T: +44 (0)161 446 3773 or
E: education.events@christie.nhs.uk

NEW
Challenges and Opportunities in Non-Medical Prescribing
9 December 2013; London, UK
W: www.royalmarsden.nhs.uk/nonmedicalprescribing
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

NEW
15th Anniversary Britain Against Cancer Conference
10 December 2013; London, UK
E: BAC@macmillan.org.uk

cancer conference
ncri
national cancer research institute

2013 NCRI Cancer Conference Trade Exhibition

List of confirmed exhibitors (as of 20th October 2013)

Exhibitor	Stand
Agilent Technologies	22
AICR (Association for International Cancer Research)	47
American Peptide Company Europe	58
Amgen	M2
AMSBIO	56
Barts Cancer Institute	52 & 53
Bioline Reagents Ltd	44
BMJ	25
Breast Cancer Campaign	68
Bristol-Myers Squibb	63
CaCTUS (Cancer Clinical Trials Unit, Scotland)	57
Cancer Research Technology	59
Cancer Research UK	S2
Cancer Research UK Centre, Southampton – CTU and ECMC	M3
Caris Life Sciences	32
Carl Zeiss Ltd	09
Celgene Ltd	49
Charles River UK Ltd	33
Children with Cancer UK	39
Cronus Technologies/Tissuegnostics	S1
ecancer	05
ESMO-European Society for Medical Oncology	2
Eurogentec	62
European Association for Cancer Research (EACR)	04
FluidX	66
GATC Biotech Ltd	41
Genomic Health	81
Hospira UK Limited	06 & 07
Illingworth Research	45
Integrated DNA Technologies	35
LGC Standards	55
LI-COR Biosciences UK Ltd 69 http://www.licor.com	
Liverpool Cancer Research UK Centre	12
Macmillan Cancer Support	79
Manchester Cancer Research Centre	46
Marie Curie Cancer Care	80
Myeloma UK	89
National Cancer Research Institute	NCRI Stand
NCRI Academic Forum for Trainees in Pathology	65
NCRI Consumer Liaison Group (NCRN)	38
Newcastle Cancer Centre	90
New England BioLabs	34
NIHR Cancer Research Network (NCRN)	36
Olink Bioscience	64
Oncology News	48
Pancreatic Cancer UK	26
Pfizer Oncology (non-exhibiting)	
Pierre Fabre Oncology	27
Prostate Cancer UK	77
Qiagen Ltd	71
Randox Laboratories Ltd	23
Roche Products Ltd	Principal
RPS Services Ltd	54
Sequenom GmbH	85
Sigma-Aldrich	51
Source Bioscience Plc	40
Target Ovarian Cancer	60
The Brain Tumour Charity	37
The British Association for Cancer Research (BACR)	87
The College of Radiographers	24
The Francis Crick Institute	50
The Institute of Cancer Researc	M4
The Royal College of Radiologists	86
The Science & Technology Facilities Council	28
UCL Cancer Institute	M1
VisualSonics	08
Wales Cancer Research Network	67
Warwick Clinical Trials Unit	61
Wisepress Bookshop	88

cancer conference
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national cancer research institute

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The ROYAL MARSDEN
NHS Foundation Trust

Education and Conference Centre Study Day Programme 2014

20 Jan	**The Royal Marsden Head and Neck Study Day**	ID 395
27 – 28 Jan	**Essential Oils in Cancer Care (2-Day Course)**	ID 337
29 Jan	**Essential Oils in Pain Management**	ID 341
30 Jan	**Essential Oils for Rest, Recovery and Repair in Cancer and Palliative Care**	ID 342
31 Jan	**Essential Oils Update Day**	ID 344
04 – 05 Feb / 09 – 10 Oct	**Foundation Skills in Oncology for Paediatric Nurses**	ID 420/421
10 Feb	**Recent Advances in Radiotherapy**	ID 352
13 Feb	**Targeted Treatments for Urological Cancers**	ID 399
04 Mar / 09 Sep	**Acupuncture for Cancer Patients Study Day**	ID 422/423
17 Mar	**National Oncoplastic Breast Surgery Study Day**	ID 419
07 Apr	**Clinical Aspects of Targeted Treatments for Lung Cancer**	ID 414
29 Apr / 11 Nov	**Introduction to Paediatric Cytotoxic Medication**	ID 424/425
13 May	**Advances in the Nutritional Care of Cancer Patients**	ID 426
07 Jun	**Everything you ever wanted to know about Lung Cancer Imaging**	ID 427
12 Jun	**Integrating Cancer Genetics into Routine Clinical Practice**	ID 429
16 Jun	**Targeted Treatments for Haematological Cancers**	ID 396
01 Jul	**Tracheostomy Care Study Day**	ID 418
22 Sep	**Targeted Treatments of the Digestive System**	ID 398
23 Sep	**The Royal Marsden Paediatric Palliative Care Study Day**	ID 431
26 – 27 Sep	**ISSC – Sexual Consequences of Cancer Treatment**	ID 432
11 Oct	**Royal Brompton Chest Radiography Study Day**	ID 251
15 Oct	**The Royal Marsden Palliative Care Update**	ID 436
21 Oct	**Psychological Support for Cancer Patients**	ID 438
05 Nov	**The Royal Marsden Gynaecological Cancers Study Day**	ID 439
24 Nov	**The Royal Marsden Haematology Study Day**	ID 443
02 Dec	**Molecular Mechanisms of Targeted Cancer Treatments**	ID 397
09 Dec	**Advances in the Nutritional Care of Cancer Patients (Repeat)**	ID 444
Dec	**Medicines Management Study Day**	ID 445
25 March 2015	**National Pain Management Study Day**	ID 413

For further information please email: conferencecentre@rmh.nhs.uk
Tel: 020 7808 2921
or visit www.royalmarsden.nhs.uk/studydays

The ROYAL MARSDEN
NHS Foundation Trust

Education and Conference Centre Conference Programme - 2014

11 Feb	**Optimising the Management of Metastatic Colorectal Cancer** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden.nhs.uk/colorectal	ID 372
09 Jun	**Multi-professional Care of individuals with Thyroid Cancer: An update on Management, Treatment, Support and Follow-up** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden,nhs.uk/thyroid	ID 417
23 – 24 Jun	**The Second Annual Pain in the Cancer Patient Meeting** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden,nhs.uk/paincancerpatient	ID 428
12 Sep	**The Royal Marsden Endometrial Cancer Conference** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden.nhs.uk	ID 430
02 Oct	**The Royal Marsden Neuro-Oncology Conference** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden.nhs.uk/neuroconference	ID 433
03 Oct	**The Seventh Annual Royal Marsden Breast Cancer Meeting: Hot Topics in Breast Cancer** The Royal College of Physicians, London, NW1 4LE www.royalmarsden.nhs.uk/breastmeeting	ID 434
10 Oct	**The Royal Marsden Bladder and Testicular Cancer Conference** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden.nhs.uk	ID 435
16 - 17 Oct	**Anaesthesia for Major Surgery Conference** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden.nhs.uk/anaesthesia	ID 437
07 Nov	**The Seventh Royal Marsden Pain and Opioid Conference** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden.nhs.uk/painconference	ID 440
14 Nov	**The Sixth Annual Royal Marsden Head and Neck Conference** The Royal College of Physicians, London, NW1 4LE www.royalmarsden.nhs.uk/headneckconference	ID 441
21 Nov	**The Second Royal Marsden Skin Cancer Conference: a GP Focus** The Royal Marsden Education and Conference Centre, London, SW3 6JJ www.royalmarsden.nhs.uk	ID 442

For further information please email: conferencecentre@rmh.nhs.uk
Tel: 020 7808 2921
or visit www.royalmarsden.nhs.uk/conferences

BTOG 2014

1st Announcement – Please save the dates

12th Annual BTOG Conference 2014

Wednesday 29th to Friday 31st January 2014 – Dublin

BTOG Chair, Dr Sanjay Popat

IMPORTANT DATES

Poster Abstract Submission Opens Online	1st September 2013
Registration Opens Online	1st September 2013
Hotel Booking Opens	1st September 2013

BTOG aims to improve the care of patients with thoracic malignancies through multidisciplinary education and encouraging the development of clinical and scientific research.

BTOG Secretariat

Dawn Mckinley, Operational Manager, British Thoracic Oncology Group (BTOG)
Glenfield Hospital, Leicester LE3 9QP UK
Tel: 0116 250 2811 • Email: dawn.mckinley@uhl-tr.nhs.uk

BTOG 2014 Information is available on the website:

www.BTOG.org

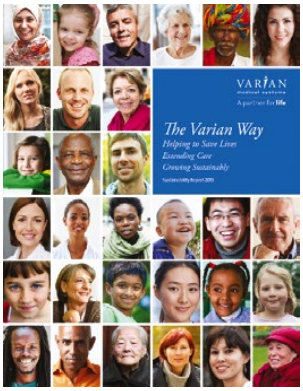
News update

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

Varian Medical Systems publishes 2013 Sustainability Report

Varian Medical Systems, a leader in radiotherapy and X-ray imaging technology, is announcing the publication of its annual corporate social responsibility report, detailing the company's policies and achievements in extending care, protecting resources, and helping to save lives. The Varian 2013 Sustainability Report has been produced as part of a wider company investment to continually improve sustainability performance and transparency.

"Companies such as ours have a responsibility to achieve our business goals in a socially and environmentally responsible manner," says Dow Wilson, chief executive officer of Varian Medical Systems. "While we continue to develop better therapeutic capabilities for fighting cancer and other diseases as well as better components for X-ray imaging and for cargo screening, we continually strive to do so in ways which extend access to advanced care, improve clinical outcomes, optimise safety, and make a positive impact on the communities where we operate."



Three years ago, Varian commenced a company-wide undertaking to examine sustainability performance and identify challenges and opportunities to be addressed over time. "We have made a commitment to produce annual updates so we could measure our achievements against defined sustainability goals." adds Wilson.

For further information contact: Neil Madle, Varian Medical Systems T: +44 (0)7786 526068 E: neil.madle@varian.com W: www.varian.com

GIOTRIF® (afatinib)* approved in Europe for patients with EGFR mutation positive lung cancer

Boehringer Ingelheim recently announced that the European Commission has granted marketing authorisation for afatinib monotherapy, for the treatment of Epidermal Growth Factor Receptor (EGFR) TKI-naïve adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutation(s). Afatinib will be marketed in Europe under the brand name GIOTRIF®.

Lung cancer is one of the most common forms of cancer, accounting for 1.6 million new cases each year.[2] It is the most deadly; more people die of lung cancer than of colon, breast and prostate cancers combined.[3] In Europe alone, lung cancer is responsible for almost 270,000 deaths each year.[4] Although incidence rates are higher in men than women it has been suggested that, by 2015, lung cancer will overtake breast cancer as the biggest cause of female cancer death in Europe.[4]

Because lung cancer is more than one disease, distinct subtypes can be characterised by receptors that are frequently altered or overexpressed in cancer cells. One such molecular marker is EGFR (a member of the ErbB Family of receptors). The prevalence of tumours harbouring EGFR mutations is between 10-15% in Caucasian and 40% in Asian NSCLC patients.[5]

For further information visit: www.boehringer-ingelheim.co.uk

References:

1. *Sequist L, Yang J, Yamamoto N, et al. Phase III Study of Afatinib or Cisplatin Plus Pemetrexed in Patients With Metastatic Lung Adenocarcinoma With Epidermal Growth Factor Receptor Mutations. J Clin Oncol 2013;DOI: 10.1200/JCO.2012.44.2806.*
2. *Ferlay J et al. Estimates of worldwide burden of cancer in 2008:GLOBOCAN 2008. International Journal of Cancer. 2010; 127 2893-2917.*
3. *American Cancer Society. What are the key statistics about lung cancer. Available at http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-key-statistics. Last accessed, September 2013.*
4. *Malvezzi M et al. European cancer mortality predictions for the year 2013. Annals of Oncology, 2013.*
5. *Jang, T.W. et al. 2009. EGFR and KRAS Mutations in Patients With Adenocarcinoma of the Lung. The Korean Journal of Internal Medicine, March; 24(1), pp.48–54.*

London Bridge Hospital unveils NEW Cancer Treatment Suite

London Bridge Hospital unveil their NEW Cancer Treatment Suite, which sees the leading HCA hospital partner with the Leaders in Oncology Care (LOC) group.

The new Cancer Treatment Suite offers state-of the-art technology, providing the very best chemotherapy and related treatments such as hormonal therapy, biological therapies and immunotherapy. Twelve individual patient pods, fitted with comfortable reclining padded chairs and a high tech screen allow patients to watch TV or check emails at their leisure, while curtains allow the option of complete privacy should patients request it.

Run by a talented, multidisciplinary team including leading Consultant Oncologists and highly skilled nurses, the new unit draws on the wider hospital to offer a one-stop approach for those diagnosed with cancer.

Dr Mark Harries, Consultant Oncologist explains, "Patients are able to follow the complete treatment pathway all on one hospital site; from initial diagnosis tests and scans, surgery and chemotherapy, to palliative care, counselling, complimentary medicine including massage, nutrition and reflexology to ease side effects, and even an on-site pharmacy. Our exceptional team of consultants, nurses, haematologists, dieticians, pharmacists and many more all work side by side to ensure patients receive the very best care."

For further information contact: www.londoncancercentre.co.uk

Elekta introduces groundbreaking image guidance capabilities integrated with Versa HD Cancer Treatment System

Integrated with Versa HD™, Elekta has introduced new intra-fraction imaging capabilities within its X-ray Volume Imaging (XVI) system. During treatment, XVI now provides the tools to monitor and manage internal motion, supporting the clinician's efforts to increase therapeutic doses delivered to the tumour while reducing healthy tissue exposure.

"Regardless of patient immobilisation, both the tumour and adjacent critical structures may move during treatment delivery. Historically, this has presented a significant challenge in delivering highly targeted treatments," says Dee Mathieson, Senior Vice President, Oncology Business Line Management. "Imaging in real time as the treatment is delivered demonstrates yet another leap forward in Elekta's long history of pioneering image guidance capabilities."

"On a second by second basis, the precise location of the tumour and sensitive healthy structures can now be visualised, helping clinicians accurately deliver dose to the tumour while minimising normal tissue exposure. It is a major advantage for patient safety and clinical effectiveness."

Uniquely, Elekta's XVI, which is also available on other Elekta radiotherapy delivery systems, includes 2D, 3D and 4D intra-fraction imaging to support live imaging during sophisticated delivery techniques, such as VMAT.

For more information, visit www.elekta.com/XVI.

A new guide to care for brain tumour patients

brainstrust has published a comprehensive, easy to understand guide to adult brain tumour care. The aim being to help patients know what to expect on their journey.

Written with clinicians, patients and carers, and compliant with NHS England's Information Standard, the guide translates the NHS and NICE 2006 Improving Outcomes Guidance (IOG) in a way that is accessible to patients. It explains:

- What happens at each point in the brain tumour pathway
- What the optimum standard of care is (according to the IOG) at each point of the pathway
- Questions to ask
- Third party support available for each stage of the journey.

The guide is written in eight easy to understand sections, each relevant to different stages of a patient's journey. It is freely available to brain tumour patients and doctors and nurses working in relevant specialties.

Clinicians may be particularly interested in sharing the guide as part of their obligation, as outlined by the IOG, to provide relevant information to patients and carers.

Consultant Neurologist, Robin Grant, says, "The most important factor that helps people keep control over their life when brain cancer strikes, is knowledge - an understanding of what is going to happen, when it is going to happen and why it is going to happen in a simple understandable way. brainstrust have set the knowledge standard in this area."

Helen Bulbeck, Director of Services for brainstrust, says, "A lot happens after you are told you have a brain tumour, and this guide will help patients and carers know what to expect and understand how to engage in their care. We know that the fight is much harder than the diagnosis and treatment - this resource will help with this."

To find out more or to request a copy, E: hello@brainstrust.org.uk or T: +44(0)1983 292405.

Exploratory data analyses of intralesional PV-10 Clinical Phase 2 Study results presented at ECC 2013

Provectus Pharmaceuticals, Inc, a development-stage oncology and dermatology biopharmaceutical company, presented detailed findings of several exploratory analyses of data from its completed Phase 2 study of intralesional PV-10 in metastatic melanoma during a Poster Session on "Melanoma and Skin Cancer" recently at the European Cancer Congress 2013 (ECCO 17- ESMO-38 - ESTRO 32) in Amsterdam, The Netherlands.

PV-10, a 10% solution of Rose Bengal that is currently under clinical investigation as a novel cancer therapeutic, is designed to selectively target and destroy cancer cells without harming surrounding healthy tissue, minimising potential for systemic side effects.

Sanjiv S Agarwala, MD, Principal Investigator for the Phase 2 trial of PV-10, and Chief of Medical Oncology and Hematology at St Luke's Hospital and Health Network in Bethlehem, PA, presented the poster which was based on Abstract No. 3.755, entitled, "Locoregional Disease Control in Metastatic Melanoma: Exploratory Analyses From Phase 2 Testing of Intralesional Rose Bengal," authored by SS Agarwala, JF Thompson, BM Smithers, MI Ross, BJ Coventry, DR Minor, CR Scoggins, JM Singer and EA Wachter.

The international, multicenter, Phase 2 study examined the effect of up to 4 treatment cycles of intralesional (IL) PV-10 in 80 subjects with AJCC Stage IIIB-IV melanoma. All subjects had locally advanced disease refractory to a median of 6 previous interventions. Intralesional PV-10 tumour ablation provided, after a median of 2 treatment cycles, rapid locoregional disease control. A high rate of response in untreated bystander lesions and transient cutaneous locoregional blistering were consistent with the novel tumour-specific immune mediated mechanism of action of PV-10.

The poster can be viewed by clicking on the following link:
http://www.pvct.com/publications/Provectus-ECCO-2013.pdf

For further please visit the Provectus website: www.pvct.com

Cancer experts detail new approaches to liver cancer treatment with stereotactic ablative radiotherapy (SABR)

Clinical experts outlined promising new approaches to treating liver cancer using radiosurgery with advanced imaging and motion management technology. Presentations on non-invasive radiosurgical approaches to treating hepatocellular carcinoma (HCC) were made by leading clinicians recently at a meeting organised by the Taiwan Society for Therapeutic Radiology and Oncology and Taiwan Liver Cancer Association.

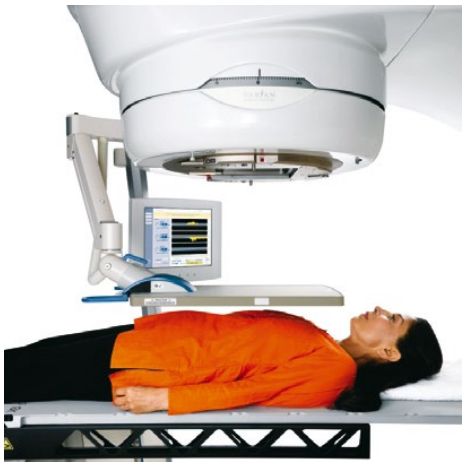
HCC, the most common type of liver cancer, is globally the third leading cause of cancer mortality after lung and stomach cancer, and a significant problem in Taiwan, mainland China, and other parts of Asia.

"Most patients with HCC are not eligible for surgery or liver transplant," said Theodore Lawrence, MD, PhD, professor and chairman of the Department of Radiation Oncology at the University of Michigan. "Historically we couldn't do much for them with radiotherapy because we lacked the ability to focus the dose on the tumour and minimise exposure of the rest of the liver. That has changed with advanced approaches like SABR."

SABR is a type of radiosurgery that involves the careful use of modern technologies for 3-D image guidance, motion management, and beam shaping. Dr Lawrence and his clinical team customise their use of SABR for each patient according to a predictive model they have developed based on treatment data from over 400 HCC cases.

For further information contact:
Neil Madle,
Varian Medical Systems
T: +44 (0)7786 526068
E: neil.madle@varian.com W: www.varian.com

Varian's Calypso tumour tracking system used in lung, stomach and prostate cancer treatments at leading European cancer centre



Clinicians in Lisbon have commenced advanced radiosurgery treatments using Varian's Calypso® 'GPS for the Body' real-time tumour tracking system. Doctors at the 'Champalimaud Center for the Unknown' (CCU) utilised the Calypso® system to enhance precision during a radiosurgery treatment that included the world's first clinical use of the new commercially available Calypso lung Beacon® transponder.

The centre has used this method to treat three patients with stage 1 non-small-cell lung cancer, according to Professor Carlo Greco, head of radiation oncology at CCU.

"Our experience so far is that tracking tumours with Calypso® transponders may help make a significant difference in lung treatments. In the past, we would have to apply a more generous treatment margin around the tumour and we would have had difficulty checking for or responding to movement caused by the patient coughing. Calypso allows us to monitor the treatment real-time and reduce the treatment margin, meaning less healthy tissue is treated."

"Calypso is a tracking and monitoring device that provides additional evidence that the dose is being delivered where it should be, which is even more important in higher dose treatments," Professor Greco added.

For further information contact: Neil Madle, Varian Medical Systems,
T: +44 (0)7786 526068, E: neil.madle@varian.com W: www.varian.com

Supporting Brain Tumour Research at Christmas

Raise funds this Christmas to support vital research into the biggest cancer killer of children and the under-40s. Help to improve outcomes for the thousands of patients and their families living with the devastating diagnosis of a brain tumour.

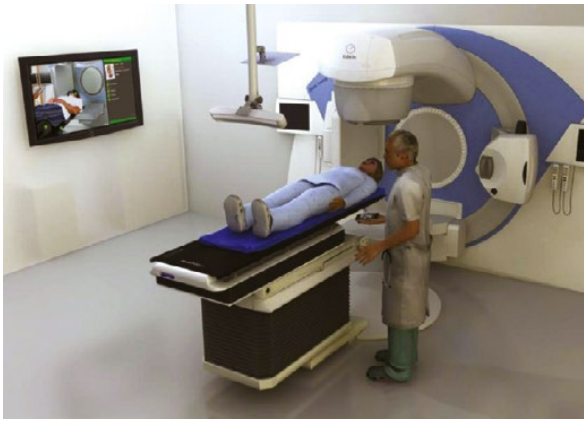
There are several ways that you can contribute. Buy and sell Christmas cards to raise funds for the charity. Every card sent is a message of hope and raises awareness of this dreadful disease. Take a box of mixed cards to sell to friends and family and / or colleagues. Host a Christmas gift event or even a fundraising Christmas dinner. Make a seasonal donation and add your 'Bauble of Hope' to the Brain Tumour Research Hope Tree at their Centre of Excellence in the University of Portsmouth. Enjoy some festive fitness – join the London Santa Run. Free Santa Suit for every runner! Details about running for charity can be found here: www.doitforcharity.com/doitforcharity-santa-run-2013.aspx

Further information about how to support Brain Tumour Research can be found on their website www.braintumourresearch.org

Switzerland's Hôpital Riviera improves confidence in treatment with Elekta's Identify™ Solution

As a new centre, Hôpital Riviera's daily radiotherapy patient volume started out small, but now averages 40 patients per day. The introduction of VMAT has resulted in a reduction in the time slot from 15-20 minutes down to 10-15 minutes, enabling a 50% increase in patients treated daily.

To ensure optimal patient and accessory identification, Hôpital Riviera has begun using Elekta's Identify™ system, bringing an additional level of confidence to patient setup.



From the moment the patient enters the treatment room, Identify verifies the right patient and the accessories required for his or her treatment. Through integration with MOSAIQ®, it gives cancer care professionals confidence by ensuring the right accessories are present for each patient's treatment session. The key to Identify™ is that it is based on advanced RFID technology, which automates the identification of the patient and accessories and provides independent verification.

To learn more about Identify, visit www.elekta.com/Identify. Identify and Versa HD are not available for sale in all markets. Please contact your local Elekta representative for more details.

Leading Academic Institutions in Bid to Become UK's Next Brain Tumour Research Centre of Excellence

Eight British universities and hospitals are in a bid to become a new Centre of Excellence dedicated to research into brain tumours. The successful institution will enter a funding partnership with the charity Brain Tumour Research, defining a new chapter in long-term sustainable research.

As part of a vision to develop seven centres in the UK, this unique strategy guarantees key salaried roles, removing limitations of project-specific grants and 'brain drain' to other areas of research where funding prospects have been more historically reliable.

The eight organisations bidding to receive funding are based in the following cities: Belfast, Birmingham, Bristol, two in London, Liverpool, Plymouth and Preston. Applications are currently being internationally peer-reviewed and the new centre will be announced by the beginning of 2014.

For more information please contact Sue Farrington Smith, Chief Executive, Brain Tumour Research sue@braintumourresearch.org

John McGirr Fund raised £35,000 for prostate cancer research

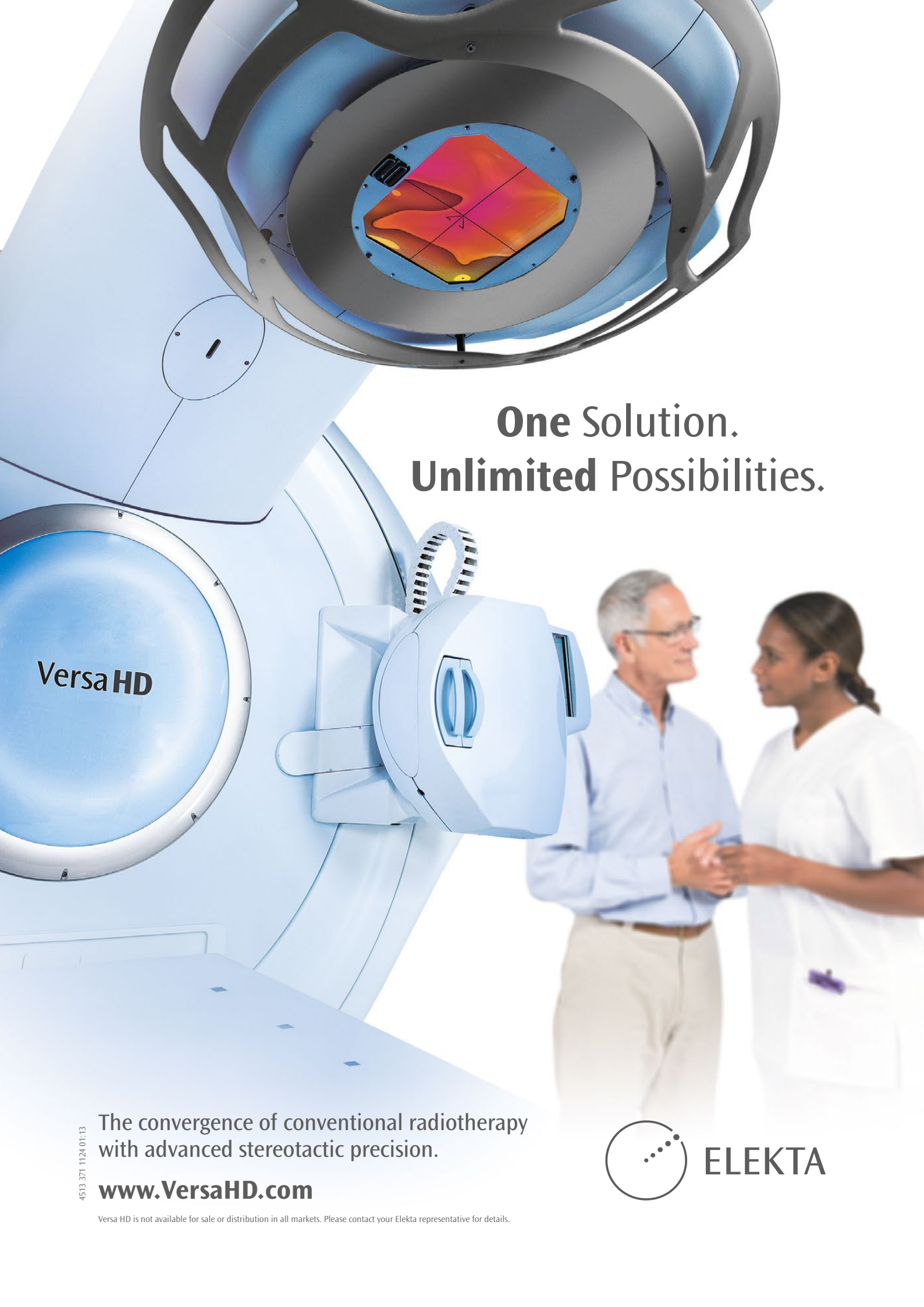
The John McGirr Fund recently donated £35,000 to support prostate cancer research. The presentation was made by Oonagh McGirr to Professor Joe O'Sullivan at the launch of the 2013 SW 200 Cycle, which will also raise money for the fund.

The money was raised by hundreds of people taking on many challenges throughout the year which included, cycling, running, swimming, playing golf and organising charity fashion shows. Oonagh paid tribute to all of those people who helped organise and participate in the wide range of fundraising activities. "Without your support the Fund would not be able to make this overwhelming contribution to the fight against Prostate Cancer, we know that there is still a great need to continue fundraising and it is our intention to continue with our efforts. Tonight we are also launching the South West 200 Cycle 2013 which is another important fundraising initiative" said Oonagh.

Joe O Sullivan, a specialist in Radiation Oncology at Queens Centre for Cancer Research and Cell Biology, was extremely impressed with the amount of money raised and explained how the donation would be used to fund the cost of researchers who are working very hard to prolong and improve the lives of those suffering with the disease. "Your efforts will make a significant difference to the quality of life of people suffering with Prostate Cancer and will give us the best possible chance of developing better treatment and eventually cures, on behalf of those people I would like to record our gratitude" concluded Joe.

The John McGirr Fund was established on March 2010 to raise money to support prostate cancer research. John McGirr was the popular owner of Sally's who passed away in December 2009.

For further information visit: www.facebook.com/JohnMcGirrFund or www.facebook.com/southwest200



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