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Oncology News

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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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Ondansetron

The first and only soluble anti-emetic film.

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

The difficulty of delivering promises: a few comments

Advances in cancer treatment and research are sorely needed. Modern technology is being applied at the clinical level based on findings at the molecular level. But is preclinical research in general simply not delivering the goods? The first item below suggests a novel technical approach that might become standard procedure in cancer surgery, and is quite a radical new approach. But advances from the "bench" that can go to the "bedside" are generally slow and have little originality, which indicates that new strategies and funding mechanisms must be considered.

Denys Wheatley, Editor.

The intelligent "cancer-smelling knife" and tumour margins

There are guidelines regarding the margin around a tumour that surgeons should follow during resection; how much normal tissue is removed to ensure all (most?) of a tumour is excised is rather subjective. Researchers at Imperial College London find they can significantly reduce the number of repeat operations by using an intelligent knife that sniffs out more objectively resection limits. iKnife detects malignant cells within normal tissue by exploiting differences in their molecular signatures (e.g. lipid composition) [1]. Analysis of >300 samples retrospectively gave results as good as traditional post-surgery diagnosis. A prospective study is clearly needed, but Lord Darzi, Professor of Surgery at Imperial College London, says its "impact on cancer surgery could be enormous."

How does it work, and will it truly deliver its promise? The iKnife is an electrothermal instrument that vaporises tissue. The fumes are sent directly into a mass spectrometer (rapid evaporisation ionisation mass spectrometry – REIMS) that detects differences in molecular composition. While the frozen section method used to check for residual tumour might take 20 or more minutes, the spectrometer coupled to the iKnife could give feedback in a few seconds. But the new procedure has yet to be put prospectively into operation, although the present retrospective comparison fits the data (exactly!) from traditional post-surgery diagnosis. But what about sensitivity, the lower limit of detection of cancer cells in normal tissue, and the problem of tumour heterogeneity? And crucially, would this make any significant difference to the current guidelines on resection margins?

Reference

1. Balog J, Sasi-Szabó L,Kinross J, Lewis MR, Muirhead LJ, Veselkov K, Mirnezami R, Dezs B, Damjanovich L, Darzi A, Nicholson JK, Takáts Z. *Intraoperative Tissue Identification Using Rapid Evaporative Ionization Mass Spectrometry.* Sci. Transl. Med. 2013;5:194ra93.

Long-term vs short-term funding of cancer research

According to Professor Peter Smith, Dean of Medicine at the University of New South Wales (NSW), if we want "to cure cancer, we need to think like venture capitalists". Cancer research needs to be more boldly tackled, with more radical ideas and inevitably greater risk. Funding of cancer research is too cosy; high risk proposals are seldom funded, and grant funding plays safe, with "small step" proposals being supported for a few years and dropped if the anticipated progress is not delivered (a short-term low-risk strategy enforced by limited budgets, and unlikely to yield potentially useful discoveries).

Peter Smith has a team developing a new treatment for neuroblastoma and melanoma [2]. An idea, abandoned by drug company support years back, has in the interim been funded for over 20 years by The Kids' Cancer Project (a charity), and now seems to be bearing fruit. A new class of drugs that targets a structure peculiar to the cytoskeleton of tumour cells causes a malignant cell to "implode". Neither the class of drugs nor the target has been disclosed, but the claim seemingly is aimed at increasing funding from the charity (with the NSW government also raising substantially its investment cancer research) to sustain this research. The drug is claimed to be effective on all cancer cells, which is at odds with well-known agents targeting the cytoskeleton (e.g. vinca alkaloids). Whether or not these promises are delivered, the point being made by Smith in a series of press releases is that long-term investment in research programmes ought to be the modus operandi rather than short-term blinkered funding.

Reference

2. http://www.watoday.com.au/comment/longer-funding-cycles-vital-in-cancer-research-20130816-2s1zz.html#ixzz2cATpWlZh

Preclinical strategies

Preclinical cancer research needs to (i) seek more novel approaches (ie be more imaginative), and (ii) deliver potential new interventions more quickly. The time from discovery to development is long, and oncologists are impatient for translation to be swifter. The main underlying problems have been explicity discussed by Bagley and Ellis [3] in an article that makes for stern reading and calls for a radical rethinking of preclinical research, its philosophy. Too many issues are raised to discuss here, such as major concerns with the piecemeal reporting of insubstantial and non-verified data (e.g. one cell line/one drug papers) on poor material rather than "robust, predictive tumour models". Concentrated and concerted input is called for, but it seems that the pleas of these and many other critics amount to little more than a few "cries in the wilderness".

Reference

3. Bagley CG and Ellis LM. *Raise standards for preclinical cancer research.* Nature 2012;483:531-3.

IF MOST OF THE PEOPLE WE HELP TODAY DON'T NEED PALLIATIVE CARE, WHAT DO THEY NEED?

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Cancer Information Development Nurse

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Cover image courtesy of Nigel McDowell.

The red-eyed leaf frog (Agalychnis callidryas) occurs throughout Central America and its skin secretion is a complex cocktail of bioactive peptides including some with anticancer properties.

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Awards and Appointments

New BNOS President to focus on brain tumours in children

At this summer's British Neuro-Oncology Society (BNOS) conference in Durham, David Walker, Professor of Paediatric Oncology at the Children's Brain Tumour Research Centre at University of Nottingham and the Society's newly appointed President, outlined his desire to focus on brain tumours in the young for the year ahead.

Professor Walker highlighted the immense consequences of brain tumours in children – the commonest form of solid tumour in the young – and its danger to life and quality of life for sufferers and survivors.

Over 70% of children who develop a brain tumour now survive the disease with improved treatments, but many suffer varying degrees of damage to their quality of life, owing to the vulnerability of the brain. Around 60% of the survivors of brain tumours in the young are moderately or severely disabled as a result and this leads to significant healthcare needs throughout their subsequent lives.

In countering the difficulties faced by children with brain tumours, Professor Walker points to the success of sustained international efforts to conduct trials of new therapies in the children over the past three decades, and the recent launch of the UK Headsmart campaign to raise awareness of the need for speed in diagnosing a tumour:

"Survival rates in children with brain tumours have increased dramatically since the 1990s when approximately 50% of children would be expected to recover. Since then, new treatments have been introduced through trials, which are saving lives. The HeadSmart Campaign seeks to accelerate diagnosis which we hope will save vision and reducing damage to dexterity and mobility." By creating a forum for the discussion of research and treatment at BNOS conferences, Professor Walker hopes to increase these success rates further across the age groups by sharing experiences of applying research into practice:

Professor David Walker

"Headsmart is the first campaign of its kind in the world and aims to speed up diagnosis of brain tumours with the aim of minimising the risk of progressive brain damage due to sustained tumour growth during delays in initiating the scans necessary for diagnosis.

"We need to understand the causes of brain tumours in the young and develop strategies to minimise the likelihood of them recurring. I'd like to see BNOS become a focus point for the discussion of research and treatment for paediatric neuro-oncology as well as adult neuro-oncology by hosting working groups and developing paediatric track in the conferences in the future. At our next conference I aim to build upon the work of Geoff Pilkington, my predecessor in expanding the scope of the BNOS conferences to include paediatric and adult nursing, as well as medical and scientific disciplines involved in brain tumour research and care across the age groups." ■

The next BNOS conference is scheduled for 9th – 11th July 2014 at Liverpool John Moores University's Art & Design Academy. Those wishing to attend or learn more about the work of the Society should contact administrator@bnos.org.uk or visit http://www.bnos.org.uk/conference.html

Pezcoller Foundation – EACR Cancer Researcher Award Lecture

Celebrating academic excellence and achievements in the field of cancer research

Nominees will be Cancer Researchers from European countries with no more than 15 years post doctoral experience and a record of employment in Europe of at least five years.

The winner will give the prestigious Pezcoller Foundation – EACR Cancer Researcher Award Lecture at EACR-23 in Munich, 5th – 8th July, 2014, and receive a prize of €10,000.

The award will be presented for the second time at EACR-23 and at future EACR biennial congresses.

Nominations are invited from scientists who are involved in cancer research or have been affiliated with any institution, cancer medicine or cancer-related biomedical science. Self nominations cannot be accepted.

Deadline for receipt of nominations: December 31st 2013. For further information visit: http://eacr23.eacr.org

New Journal Reviewer for Oncology News

Dr Sunil Upadhyay is a Consultant Clinical Oncologist at Queen's Centre for Oncology, Castle Hill Hospital, Hull. He graduated from Lucknow, India. After post-graduate training in Clinical Oncology from Delhi University, he had further training at Beatson Cancer Centre, Glasgow and Royal Berkshire Hospital, Reading before coming to Hull in 1992. His main areas of interest are the management of breast and lung cancers. He is a senior clinical tutor for undergraduate medical students from Hull & York Medical School and post graduate trainees in clinical oncology. He has a keen interest in research and has been principle investigator for many trials. He has been speaker at many oncological meetings/conferences and has over 100 publications in national & international journals. He has been Clinical Director of the QCOH and Chairman of the Joint Hospital Medical Staff Committee, HEY. He is member of many national and international cancer organisations. Currently, he is Chairman of the North of England Oncology Association and Secretary of the East Yorkshire Oncology Association. He has also been on expert advisory boards for many pharmaceutical companies. Dr Upadhyay will join the Journal Review Panel reviewing the following journals for us: *The Lancet, the International journal of Radiation Oncology and New England Journal of Medicine.*

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- Therapeutic dose attainable after 1 week[1]
- Available as tablets, syrup and solution for infusion[1]

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(Please consult the Summary of Product Characteristics (SPC) before prescribing.)

Vimpat®
Lacosamide

Active Ingredient: *Tablets:* Lacosamide 50 mg, 100 mg, 150 mg and 200 mg. *Syrup:* Lacosamide 10 mg/ml. *Solution for infusion:* Lacosamide 10 mg/ml.

Indication:

Vimpat is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent (16-18 years) patients with epilepsy.

Dosage and Administration:

Adults and adolescents from 16 years: Vimpat must be taken twice a day. Recommended starting dose is 50 mg twice a day which should be increased to an initial therapeutic dose of 100 mg twice a day after 1 week. Lacosamide treatment may also be initiated with a single loading dose of 200 mg, followed approximately 12 hours later by a 100 mg twice daily (200 mg/day) maintenance dose regimen. A loading dose may be initiated in patients in situations when the physician determines that rapid attainment of Lacosamide steady state plasma concentration and therapeutic effect is warranted. It should be administered under medical supervision with consideration of the potential for increased incidence of central nervous system adverse reactions (see sec 4.8 of SPC). Administration of a loading dose has not been studied in acute conditions such as status epilepticus. Maximum daily dose of 400 mg (in two 200 mg doses). For *solution for infusion:* Infused over a period of 15 to 60 minutes twice daily. Can be administered i.v. without further dilution. For *Syrup:* Only the measuring cup provided in the pack should be used for dosing of Vimpat syrup 10 mg/ml. *Elderly:* No dose reduction necessary. Age associated decreased renal clearance with an increase in AUC levels should be considered. *Paediatric patients:* Not recommended. *Patients with renal impairment:* No dose adjustment is necessary in mildly and moderately renally impaired patients (CLCR>30 ml/min). In patients with mild or moderate renal impairment, a loading dose of 200 mg may be considered, but further dose titration (>200 mg daily) should be performed with caution In patients with severe renal impairment (CLCR ≤30 ml/min) and in patients with end-stage renal disease, a maximum maintenance dose of 250 mg/day is recommended. In these patients, the dose titration should be performed with caution. If a loading dose is indicated, an initial dose of 100 mg followed by a 50 mg twice daily regimen for the first week should be used. *Patients with hepatic impairment:* No dose adjustment needed in mild to moderate impairment A loading dose of 200 mg may be considered, but further dose titration (>200 mg daily) should be performed with caution. In accordance with current clinical practice, if Vimpat has to be discontinued, it is recommended this be done gradually (e.g. taper the daily dose by 200 mg/week).

Contraindications, Warnings, etc.:

Contraindications: Hypersensitivity to Lacosamide or to any of the excipients. Known second-or third-degree atrioventricular block. Precautions: Lacosamide has been associated with dizziness. Use with caution in patients with known conduction problems, severe cardiac disease or in elderly. Second degree or higher AV block has been reported in post-marketing experience. Atrial fibrillation or flutter has been reported in open-label trials and in post-marketing experience. Patients should be made aware of the symptoms of second-degree or higher AV block and of the symptoms of atrial fibrillation and flutter (e.g. palpitations, rapid or irregular pulse, shortness of breath). Patients should be counseled to seek medical advice should any of these symptoms occur. Monitor patients for signs of suicidal ideation and behaviours. Advise patients and carers to seek medical advice should such signs emerge. *Interactions:* Prolongations in PR interval with Lacosamide has been observed in clinical studies. Use with caution in patients treated with products associated with PR prolongation and those treated with class I antiarrhythmic drugs. Strong enzyme inducers such as rifampicin or St John's Wort may moderately reduce the systemic exposure of Lacosamide. No significant effect on plasma concentrations of carbamazepine and valproic acid. Lacosamide plasma concentrations were not affected by carbamazepine and valproic acid. No clinically relevant interaction with Ethinylestradiol and Levonorgestrel. No effect on pharmacokinetics of digoxin. *Fertility, pregnancy and lactation:* Should not be used during pregnancy. For precautionary measures, breast feeding should be discontinued during treatment with Lacosamide. *Driving etc.:* Patients are advised not to drive a car or operate other potentially hazardous machinery until they are familiar with the effects of Vimpat on their ability to perform such activities.

Adverse Effects:

Very common (≥10%): Dizziness, headache, diplopia, nausea. Common (between1%-10%): Depression, confusional state, insomnia, balance disorder, abnormal coordination, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, hypoesthesia, dysarthria, disturbance in attention, blurred vision, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability, injection site pain or discomfort, irritation, fall, skin laceration. The use of Lacosamide is associated with doserelated increase in the PR interval. Adverse reactions associated with PR prolongation may occur. Please consult SPC in relation to other side effects.

Pharmaceutical Precautions:

Tablets: None. *Syrup:* Do not refrigerate. *Solution for infusion:* Do not store above 25°C. Use immediately.

Legal Category: POM

Marketing Authorisation Number(s):

50mg x14tabs: EU/1/08/470/001; 100mg x14tabs: EU/1/08/470/004; 100mg x 56tabs: EU/1/08/470/005; 150mg x14 tabs: EU/1/08/470/007; 150mg x 56tabs: EU/1/08/470/008; 200mg x 56 tabs: EU/1/08/470/011; Syrup: (10 mg/ml) x 200ml: EU/1/08/470/018; Solution for Infusion (10 mg/ml) x 20 ml: EU/1/08/470/016.

UK NHS Cost:

50 mg x 14 tabs: £10.81; 100 mg x 14 tabs: £21.62; 100 mg x 56 tabs: £86.50; 150 mg x 14 tabs: £32.44; 150 mg x 56 tabs: £129.74; 200 mg x 56 tabs: £144.16; Syrup (10 mg/ml) x 200ml; £25.74; Solution for Infusion (10 mg/ml) x 20 ml: £29.70.

Marketing Authorisation Holder:

UCB Pharma SA, Allée de la Recherche 60, B-1070 Brussels, Belgium.

Further information is available from:

UCB Pharma Ltd, 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom.
Tel: +44 (0)1753 534655. Fax: +44 (0)1753 536632.

UCB (Pharma) Ireland Ltd, United Drug House, Magna Drive, Magna Business Park, City West Road, Dublin 24, Ireland.
Tel: +353 14637395. Fax: +353 14637396.

Email: medicalinformationuk@ucb.com Date of Revision: 03/2013 (UK/13VPE0022). Vimpat is a registered trademark

UK Specific Information:

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 UCB Pharma Ltd.

References:

1. VIMPAT® Summary of Product Characteristics.

Date of preparation: May 2013
UK/13VPE0037

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

British Neuro-oncology Society Annual Meeting

Date: 10-12 July, 2013. **Venue:** Durham, UK.

This year marked the 33rd meeting of the British Neuro-oncology Society (BNOS), held at The University of Durham, nestled in the heart of extraordinary countryside. The focus of the meeting was 'art and science', reflecting the extensive collaboration which is needed between clinicians, scientists and patients to take forward the care and treatment of those affected by brain tumours.

BNOS is continually evolving, which is apparent with innovations implemented at each annual meeting. This year's meeting continued this tradition with the introduction of a formal full day, parallel program for nursing and allied health professional delegates. However, in keeping with custom, the official conference programme was proceeded by an education day, in which a comprehensive overview of 'The Molecular Biology of Tumours' was presented for clinicians and 'Understanding the pathway of care for a patient with glioblastoma multiforme' was directed for pure scientists. As usual, the education day ensured plenty of basic and clinical science diversity.

The quick fire five minute poster orals and short oral presentations provided an excellent start to the conference and an ideal way for investigators to disseminate an overview of their work to an audience not always familiar with basic science or clinical practises. The exceptional array of presentations kept these sessions innovative and ensured that there was a plethora of compelling discussions to be had over the evening entertainment, including a guided tour of and dinner at the breathtaking Durham castle.

Other highlights from the meeting included an incredible Brain Tumour Research sponsored plenary lecture – 'Analysis of genome and epigenome to guide clinical trials in paediatric neurooncology' – from Dr Cynthia Wetmore, Director of Molecular Clinical Trials at St Jude Children's Hospital, who demonstrated how current sequencing stratifications of the genome and epigenome of paediatric brain tumours is used to identify actionable targets in clinical trials; and an outstanding inaugural Stephen Baker Memorial Lecture, sponsored by the Brain Tumour Research Charity – 'Personalised neuro-surgery for gliomas – where are we at?' from Professor Jöerg-Christian Tonn, Director of the Department of Neurosurgery, University Hospital, Ludwig-Maximilians-University Munich, providing a concurrent overview of the contemporary techniques and understanding of glioma biology necessary to personalise glioma surgery. Furthermore, Dr Mary Lovely, Assistant Adjunct Professor at the University of California, San Francisco, School of Nursing, delivered an exceptional keynote lecture, sponsored by BrainsTrust, entitled 'Effects of Low grade Gliomas on Patients and Families'.

The mixture and choice of presentations at the conference covered the full range of multidisciplinary involvement, ranging from 'The Selective Targeting of Brain metastases' to 'Pregnancy in Women with Glioma' to 'Radiation versus Observation following surgical resection of Atypical Meningioma'.

This year's meeting also witnessed the inauguration of Professor David Walker as the new president of BNOS, with Dr David Jellinek as the new Vice-President and Professor Silvia Marino as Honorary Secretary. The 33rd Annual Meeting of BNOS is scheduled to be held at Liverpool John Moores Art and Design and Academy from 9th – 11th July 2014. See www.bnos.org.uk for more information. ■

Report by Dr Laura K Donovan, BNOS post-graduate rep and Senior Research Associate, Department of Cellular and Molecular Neuro-oncology, Portsmouth University, Portsmouth, UK.

PinkDrive and Dis-Chem open their doors to Norwood women

PinkDrive, in association with Dis-Chem Pharmacies and The Dis-Chem Foundation, provided free mammographic services to medically uninsured women at the Dis-Chem Pharmacy in Norwood in honour of National Women's Day.

"Following worldwide cancer statistics, breast cancer is the most prevalent cancer in women of all age groups in South Africa, with a staggering 1 in 29 chances of developing some form of breast cancer in a women's lifetime. With this in mind, The Dis-Chem Foundation approached PinkDrive to help them in creating a new joint initiative that will focus on educating women about breast health and promoting breast cancer awareness." says Noelene Kotschan, PinkDrive Founder and Director.

Registered and certified mammographers provided mammographic services to 28 women on the PinkDrive Mobile Mammography Unit, while a PinkDrive nurse performed 45 free clinical breast examinations throughout the day. In-store and outside the Norwood Dis-Chem Pharmacy entrance, everything was geared towards women, with all staff wearing pink, pink treats and neutrapeutical stalls.

"The Dis-Chem Foundation is committed to helping those in need, along with PinkDrive. The foundation will be assisting in the facilitation of providing mammograms, because every woman deserves one." says Trisch Rosema Trustee of The Dis-Chem's Foundation.

The next joint wellness day will be at the Vaal Dis-Chem Pharmacy on 22 October 2013. Visit www.pinkdrive.co.za for more information.

Gliolan® 30 mg/ml powder for oral solution.
Qualitative and quantitative composition: One vial contains 1.17 g of 5 aminolevulinic acid, 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).
Contraindications: Hypersensitivity to 5-aminolevulinic acid hydrochloride or porphyrins; acute or chronic types of porphyria; pregnancy.
Undesirable effects: Adverse reactions observed after the use of Gliolan® for fluorescence-guided glioma resection are divided into the following two categories: Immediate reactions occurring after oral administration of the medicinal product before induction of anaesthesia (= active substance-specific side effects); combined effects of 5 ALA, anaesthesia, and tumour resection (= procedure-specific side effects). Frequency: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000); very rare (≤ 1/10,000).
Substance-specific side effects: *Uncommon:* Hypotension; nausea, photosensitivity reaction, photodermatosis.
Procedure-related side effects: The extent and frequency of procedure-related neurological side effects depend on the localisation of the brain tumour and the degree of resection of tumour tissue lying in eloquent brain areas. *Very common:* Anaemia, thrombocytopenia, leukocytosis. Blood bilirubin, Alanine aminotransferase, Aspartate Aminotransferase, Gamma glutamyltransferase or Blood amylase increased. *Common:* Neurological disorders (e.g. hemiparesis, aphasia, convulsions, hemianopsia). Thromboembolism. Vomiting, nausea. *Uncommon:* Hypotension. *Very rare:* Hypesthesia; diarrhoea. One case of moderate chills; one respiratory insufficiency after overdose, which resolved completely.
Legal classification: POM (prescription only medicine).
Price per vial: €980/ £950 ex. factory Marketing authorisation number: EU/1/07/413/001-003
Marketing authorisation holder: medac GmbH, Fehlandtstraße 3; D-20354 Hamburg.
Date of revision of text: 09/2007
Gliolan has been authorised in all countries of the EU as well as in Iceland and Norway.

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to medac drug safety at: drugsafety@medac.de

medac code: medacuk 017/04/2012
Date of Preparation: April 2012

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Gliolan, for the visualisation of malignant tissue during surgery for malignant glioma (WHO grade III and IV) in adult patients.

gliolan® seeing is the beginning

Beatson International Cancer Conference "Targeting the Tumour Stroma"

Date: 7-10 July 2013. **Venue:** Glasgow, UK.

The first day of the Beatson International Cancer Conference was held at the Beatson Institute for Cancer Research and was started with warm weather and a warm welcome by director Karen Vousden and organiser Jim Norman. This year's conference was entitled: "Targeting the Tumour Stroma", and the first speaker of the day was Dario Neri, who introduced us to the use of antibodies and antibody-fragments to specifically deliver drugs to the tumour. These antibodies can deliver cytokines like TNF-α and IL-2 to harness the immune system to clear tumour mass. He described the successful use of antibodies directed against cancer specific splicing isoforms of the matrix constituent fibronectin as a potential treatment in in vivo models. The highlight of the day was keynote lecturer, Prof Dr Robert Kerbel, who was awarded the Colin Thomson Memorial Medal for his lifetime achievements in developing animal models that closely resemble human cancer progression and metastasis.

The remaining days of the conference where held at Glasgow University in the Bute hall. Monday morning's topic was the role of tumour vasculature, where people discussed how tumours and their surrounding stroma promote angiogenesis and how to target this. Kari Alitalo showed that the orphan receptor Tie1 is crucial for tumour angiogenesis and that Tie-1 knockout mice exhibit reduced tumour growth. Although Tie1 is a potential drug target, combinational targeting of tie-1 and VEGF/VEGFR had no additional or synergistic effects. Valerie Le Bleu presented the highly novel an provocative finding that metastatic dissemination has quite particular bioenergetic requirements, showing that changes in the tumour microenvironment impact on cancer metabolism to favour dissemination. Massimiliano Mazzone showed that the tyrosine kinase receptor Met is increased in infiltrating neutrophils due to tumour-derived factors such as TNF-α and it is required for their anti-tumoural activity. However, Met inhibition in tumour cells reduces tumour growth.

In the afternoon we shifted gears to the role of the metastatic niche in cancer. One of the highlights of this afternoon was Gustavo Leone, who argued for co-evolution of neoplastic cells together with stromal cells. He showed that PTEN knockout in stromal fibroblasts is enough to drive hyperplastic lesions in the mammary gland, and expression of ERBB2, but not Ras, in the mammary epithelium together with stromal PTEN depletion results in oncogenic lesions that closely resemble human tumours.

Jim Norman and Robert Kerbel

Tuesday morning started with Alexander Anderson, who used mathematical models consisting of melanocyes, keratinocytes and fibroblasts to recapitulate the in vivo skin. By manipulating variables in his model he was able to show that senescent fibroblasts could drive melanoma formation. This model may be a powerful tool to investigate how therapeutic intervention could restore normal skin homeostasis. Fibroblasts can be converted into cancer-associated fibroblasts (CAF) by soluble factors released by the tumour, like TGF-β. CAFs facilitate extracellular matrix stiffening, and Eric Sahai showed that contractile forces exerted by stiffened ECM activate the transcriptional co-regulator YAP, which keeps the CAFs in an activated state via ROCK-1/2. ROCK inhibitors can break this feedback loop and revert CAFs to a more normal state. Furthermore, Valerie Weaver, described that ECM stiffening results in activation of β-catenin and Myc, which causes up regulation of the mir-17-92 cluster. This cluster downregulates HogA9 in breast tumours, and re-expression of HoxA9 normalises breast tissue architecture.

This year's poster session was very diverse with over a hundred posters and initiated enthusiastic discussions between delegates. Two posters were awarded prizes: Thomas Cox with his presentation on the role of hypoxia-driven secretion of Lysyl oxidase in metastatic bone lesions, and Jean Albrengues with his findings on LIF cytokine release by CAFs to form a pro-invasive tumour environment. This day was concluded with the conference dinner where people were treated to the national Scottish dish 'Haggis' followed by a Ceilidh (traditional Scottish dancing).

The final day focussed on the role of inflammation in tumour development. Nata Erez was awarded the AMSBIO-Trevigen award for her excellent short talk on the capacity of cancer-associated fibroblast to recruit immune cells that promote tumour-angiogenesis. Paul Martin has shown that neoplastic cells have frequent interactions with neutrophils driven by hydrogen peroxide, an important chemo-attractant in wounded tissue. He showed that these immune cells release trophic factors such as prostaglandins that promote proliferation, and he therefore proposed that future research should focus to nudge immune cells to kill neoplastic cells instead of nurturing them. Florian Greten showed that the unfolded-protein response is a novel non-canonical drive for tumour-dependent NFκB-activation via IKKα. He showed that activation of the Wnt-pathway in combination with NFκB-activation could drive tumourigenesis in intestinal non-stem cells. Lars Zender concluded the conference with his presentation on immune surveillance of senescent pre-neoplastic hepatocytes. CD4+-T-cells require macrophages for clearance of senescent hepatocytes, and these macrophages depend on CCL2 (MCP-1)-induced chemotaxis for homing and senescent cell-clearance. He also developed a very interesting screen using an in vivo transposon-based shRNAi library to identify p38-MAPK as a target for combinational treatment with Sorafenib. With these exciting findings and with the announcement of the next Beatson International Cancer Conference, entitled "Powering the cancer machine" (6-9 July 2014 (www.beatson.gla.ac.uk/Conference.html)), we concluded this successful and diverse conference. ■

Report by Peter V.E van den Berghe & Elena Rainero, Beatson Institute for Cancer Research, Glasgow, UK.

2013 NCRI Cancer Conference: Programme highlights

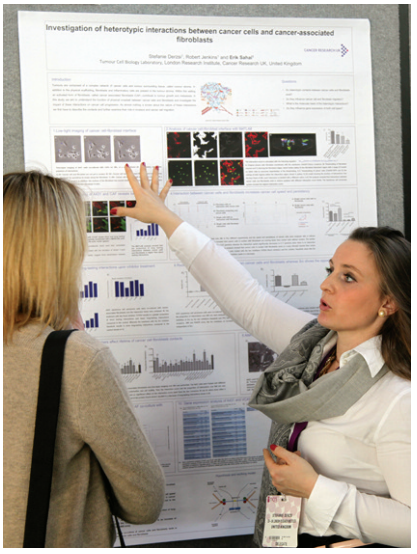
Date: 3-6 November, 2013. **Venue:** Liverpool, UK. **PREVIEW**

Liverpool's reputation as a vibrant international city where innovation flourishes has been demonstrated over the centuries. It is fitting that it should once again host the leading cancer research meeting in the UK. From 3–6 November, 2,000 cancer research professionals are expected at the award-winning BT Convention Centre, to network and learn from their peers.

The NCRI Cancer Conference combines the best basic, clinical and translational research from around the world and the UK, offering a unique overview of the latest advances across disciplines – ranging from diagnosis to treatment, basic research, prevention, survivorship and more.

Eleven plenary speakers, world leaders in their fields, have been chosen by the scientific committee. They include Nazneen Rahman speaking about her research in genetic predisposition to cancer, Charles Swanton on mechanisms of drug resistance, and Frances Shepherd discussing her research on treatments and clinical trials for lung cancer.

More than 150 speakers, and more than 50 sessions – symposia, parallel sessions, workshops, proffered paper sessions, poster discussions and clinical trials showcases as



well as structured networking events – have been designed to give each participant the chance to tailor the programme to their needs. Sessions like 'Review of targeted therapies'; 'Smarter surgery for better cancer outcomes'; 'Application of nanotechnology to oncology'; and, 'Cancer immunology and immunotherapy: Building on success' are scheduled to showcase innovative research from the UK and the world. Other clinical highlights feature in sessions on brain cancer, neuroendocrine tumours, sarcoma and paediatric oncology, as well as a special radiotherapy programme track organised in association with the Royal College of Radiologists on Tuesday 5 November.

Ninety-five percent of 2012 participants said they would recommend the meeting to a friend. The strength of the 2013 programme, and the associated social events, will once again ensure that participants leave the meeting refreshed and re-energised, with many having formed new collaborations in their field and beyond.

As Prof Gerard Evan, Head of Department of Biochemistry, University of Cambridge, UK and Chair of the 2013 NCRI Cancer Conference Scientific Committee, puts it: "If you want to understand cancer, and you want to help people with cancer, then this is the place to go. You will have the opportunity to talk with anybody from anywhere. It doesn't matter what level you are at, we are all equal." ■

To find out more and register, visit http://conference.ncri.org.uk.

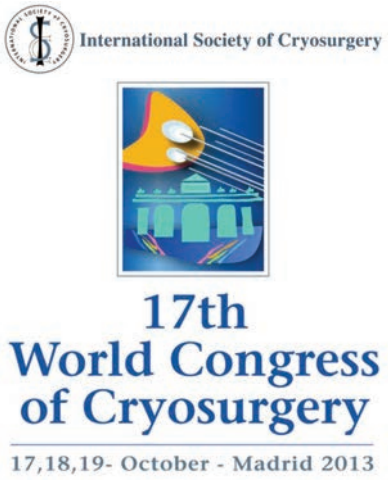
17th World Congress of Cryosurgery

Date: 17-19 October, 2013. **Venue:** Madrid, Spain. **PREVIEW**

The 17th World Congress of Cryosurgery will be held at the Gran Hotel Ayre Colon and at the University Hospital Gregorio Marañón, in the exciting city of Madrid, in October this year.

The aim of this conference is to maintain the scientific rigor and encouragement that characterises the International Society of Cryosurgery, while also pledging our commitment to relevant medical topics, which will no doubt create intense debate.

The Organising and Scientific Committees had put interest, effort and enthusiasm at their maximum so that the scientific program and the activities to be carried out match all attendees' expectations. The topics that will be covered are: Cryosurgery in prostate, bronchial, liver, renal, pancreatic and bone cancer; the role of immunotherapy and cryotherapy; dendrytic cells and their possibilities in cryosurgery; cryotherapy in the biochemical relapse after



radiotherapy and abstracts session, where the most recent advances will be presented.

In this particular occasion, the ISC thought is to exchange different experiences and expertise not only among colleagues but also among others coming from different medical specialties, so that we can learn from each other.

On the other hand, you will have the opportunity to experience the cosmopolitan city of Madrid, which offers us its attractiveness and its quality services. The city of Madrid and the Hospital Gregorio Marañón will provide us with a unique scenario for this Congress, thanks to the generous, functional and comfortable premises of this prestigious hospital, and, to the long-term experience in organising scientific activities that Dr Hernández's staff has. We look forward to see you at the ISC Congress and to have a nice staying in Madrid. ■

For further information visit:
http://www.societyofcryosurgery.org/

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Can Some HER2-Positive Breast Cancers be Considered as Low Risk?

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Breast cancer is globally the most frequently diagnosed cancer and the leading cause of cancer death in women. There were 49,564 new cases and 11,556 deaths from breast cancer in the UK in 2010. The management of breast cancer has always been controversial, mainly because of wide interest in its emotiveness, resulting in extensive research and better knowledge of the condition. Clinical presentation, stage of the disease and individual preferences has always played an important role in the choice of primary therapy, particularly the selection of adjuvant treatments. With an increasing understanding of tumour biology, the goal-posts have moved. By the application of genomic analyses, breast cancer can be seen as a heterogeneous, phenotypically diverse disease composed of many subtypes (luminal-A, luminal-B, erbB-2 positive and basal, and others) that can have their own distinctive behaviour. This has resulted in careful selection of interventions, with more limited toxicity and improved outcome – one of the best examples of personalised medicine.

Amplification and/or overexpression of the human epidermal growth factor receptor-2 (HER2-) oncogene occur in ~20 percent of primary invasive breast cancers. They have been associated with aggressive behaviour, increased proliferation, motility, invasiveness, progressive regional and distant metastases, accelerated angiogenesis and reduced apoptosis, all of which give a poor prognosis. Anti-HER2-agents (e.g. trastuzumab) have revolutionised the management; its routine use is now standard of care in combination with neoadjuvant chemotherapy for patients with tumours >1cm (>T1c). However, after a decade following landmark trials in ASCO 2005 that established the efficacy of adjuvant trastuzumab, the management of smaller (≤1cm), HER2-positive tumours continues to be a major challenge. NICE guidelines simply state that trastuzumab treatment should be considered as an option for women with early-stage HER2-positive breast cancer after surgery, chemotherapy and occasionally radiotherapy [1]. Some uncertainties in these guidelines have resulted in ongoing debates among clinicians, leading ultimately to a wide variation in subjective judgement-based management.

The traditional view has been that patients with T1a/b (≤1cm) tumour have an excellent long-term outcome and therefore do not benefit from further adjuvant cytotoxic therapy. This has certainly been the accepted norm for hormone receptor-positive tumours that are considered relatively chemotherapy resistant [2,3]. However, a minority of this group of patients relapse. With present day molecular profiling, the concept of high- and low-risk categories has emerged in patients with tumours of ≤1cm [4]. Evidence is lacking regarding the benefits from systemic therapy for these patients, because either the HER2-positive status is unknown in the historical adjuvant chemotherapy trials or these lower risk populations have not been included in the large randomised trials of adjuvant trastuzumab. Unfortunately, the web-based decision-making tools such as Adjuvant online, Predict, Oncotype DX® and MammaPrint®, are little help.

Very little data is available from prospective trials on the adjuvant treatment of small (≤1cm), node-negative breast tumours. Whilst such patients generally have a favourable prognosis, clinicians continue to explore strategies for excellence. The evidence in support of the use of adjuvant chemotherapy and trastuzumab in Ta/b HER2-positive tumours is based largely on retrospective studies and subset analyses from randomised trials. HER2-positive tumours seem to be more sensitive to aromatase inhibitors than tamoxifen in post-menopausal women [5,6]. Therefore, one may conclude that adjuvant trastuzumab therapy will give little advantage considering its acute and late side effects.

As early as 2009, Rodrigues et al. [7] presented results from a small multicentre retrospective stud suggestive of a high recurrence rate (7% at 25 months follow-up), including one death in the T1b tumours without adjuvant chemotherapy and/or trastuzumab. However, all the relapsed patients had hormone receptor-negative tumours. Updated results at 41 months (2011) showed that there was no invasive recurrence in the trastuzumab treated group, but 8 of the 56 patients not receiving trastuzumab had recurrent invasive disease (100% vs 89%; $p = 0.02$) including deaths [8].

Two retrospective studies have indicated that patients with a T1a/bN0M0 HER2-positive tumour are at a higher risk of recurrence (2-5 fold) and might benefit from adjuvant trastuzumab [9,10]. The US study [9] also identified an increased risk of metastasis among women with small HER2-positive tumour, compared to those with HER2-negative tumours. Dr Gonzalez-Angulo et al. [9] reviewed records from 965 women with T1a/bN0M0 diagnosed between 1990 and 2002, with a median follow-up of six years. They found that 77% of the HER2-positive patients had no recurrence five years after diagnosis, with 86% free of metastasis, compared with 94 and 97% of the HER2-negative patients, respectively. Women with HER2-positive tumours were 2.7 folds more likely to have a recurrence and 5.3 fold more likely to develop metastasis than women with HER2-negative tumours [9].

In the European study, Dr Curigliano et al. [10] reviewed records from 2,130 women treated between 1999 and 2006 for tumours of 1cm or less in diameter that had not spread to the lymph nodes. Of these women, 150 (7%) had HER2-positive disease. After a median follow-up of 4.6 years, HER2-positive disease was associated with less favourable disease-free survival, regardless of receptor status. Among women who were hormone receptor-positive, five year disease-free survival was 92% for patients with

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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 and male patients with female partners of childbearing potential must 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

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RXUKMEDI00117 Date of Preparation**: January 2013**

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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 UK Drug Safety Centre on: 01707 367554.

Reference: 1. PERJETA Summary of Product Characteristics. March 2013.
Date of Preparation: February 2013 RXUKPERT00028n

Table 1: Follow-up and outcomes

	All patients			Subset of patients with tumour ≤ 10mm		
3-year	No Trastuzumab (n=106)	Trastuzumab (n=155)	p-value	No Trastuzumab (n=45)	Trastuzumab (n=54)	p-value
Loco-regional RFS	92%	98%	0.014	92%	96%	0.30
Contra-lateral RFS	98%	100%	0.082	97%	100%	0.26
Distant RFS	95%	100%	0.008	97%	100%	0.30
DFS	82%	97%	0.0001	78%	95%	0.02
Overall Survival	97%	99%	0.18	98%	98%	0.75

HER2-positive tumours and 99% with HER2-negative tumours. In patients with hormone receptor-negative disease, disease-free survival was 91% and 92%, respectively.

To address the potential role of trastuzumab in low-risk patients mostly excluded from key randomised, adjuvant trials, a retrospective analysis of those with ≤2cm node-negative but HER2-positive breast cancer who did or did not receive adjuvant trastuzumab therapy has been reported [11]. The decision to use trastuzumab was time-dependent (pre- vs post-reporting of the adjuvant trials), possibly minimising uncontrolled confounding factors. A cohort of 106 patients diagnosed before May 2004 which was not treated with trastuzumab, and another cohort of 155 patients diagnosed after May 2005 which was treated with trastuzumab, were included.

Table 1 summarises the recurrence-free and overall survival data at three years. The major limitation of the study is that it does not provide information as to how much of the benefit can be ascribed specifically to trastuzumab vs chemotherapy. However, the trastuzumab treated cohort may have been at a slightly higher overall risk of recurrence because of slightly larger tumour size and a higher proportion of women with lympho-vascular invasion.

These findings are consistent with the ESMO guidelines which states, that while randomised trials have excluded patients with small primaries of < 1cm, overexpression of HER2 results in a poorer prognosis even in the case of small tumours, and the use of trastuzumab should be discussed with women with small, node-negative breast cancers [12]. Similarly, the recently updated National Comprehensive Cancer Network (NCCN) guidelines also recommended considering adjuvant trastuzumab for node-negative tumours measuring 0.5–1.0cm (T1bN0) given their potentially aggressive biology and uncertain relapse risk [13].

Thus most T1a/b breast cancers have a good prognosis and adjuvant chemotherapy is not routinely recommended. However, retrospective data suggests that some small HER2-positive cancers might have a worse clinical outcome than others. This raises the important question of whether patients with small HER2-positive cancers should be offered adjuvant trastuzumab and chemotherapy. Pivotal adjuvant trastuzumab trials did not include patients with tumours ≤1cm, but subset analysis of adjuvant HERA trial shows that patients with 1-2cm cancers derived at least as much clinical benefit from 1 year of adjuvant trastuzumab with chemotherapy as the overall cohort.

Another question debated is the role of adjuvant anti-HER-2 treatment without administration of adjuvant chemotherapy for small tumours, which may be acceptable to patients as well as clinicians. There is ample clinical data, in both metastatic as well as neo-adjuvant settings, suggesting that there is a subgroup of patients in which anti-HER-2 therapy alone is sufficient to achieve good response rates and be as effective as with additional chemotherapy. The current adjuvant subcutaneous trastuzumab SafeHer trial may soon shed some light on this because 10% of the patients with ≤1cm tumour will be randomised without chemotherapy. Shorter duration of adjuvant trastuzumab is seen as an alternative, following the publications of FinHer [14] and PHARE trial [15], with the results from the Persephone trial on the duration issue being eagerly awaited.

Ongoing research should help to resolve some of these questions, but may raise a few more. While there is no prospective trial data for smaller HER2-positive tumours, currently available evidence suggests that those with small tumours will merit individual consideration; discussions of the risk benefit ratio with the patients would be appropriate. There is an urgent need to develop methods to identify factors that might provide more information to help patients and clinicians address these difficult issues. ■

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Amphibian Skin Venoms as a Potential Source of Anticancer Drug Leads

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The pharmaceutical/biotechnology industry is currently focused on the development of biological drugs, often based upon nucleic acids or proteins/peptides – the very molecules that are fundamental to the life process in all organisms and with which all cells are familiar and have been since life began. Monoclonal antibodies (proteins) and small inhibitory RNAs (nucleic acids) are 2 major novel classes of contemporary biological drugs [1,2]. The former have provided some frontline anticancer drugs, such as Avastin. Another source of such biological drugs is animal venoms, which initially seems counter-intuitive, for, after all, these contain toxins that can either debilitate or kill. However, this is exactly what we wish to do to the cancer cells while sparing normal cells – achieving highly-selective targeting while causing minimal collateral damage – something that most current anticancer drug regimes fail to do. Intriguingly, this is exactly the major attribute of many component toxins in venoms, ie to be highly-specific in their targeting. Thus these toxins might be another class of so-called "smart" weapons in the fight against cancer.

Reptile venoms have been the most studied to date and have yielded the lead molecules for ACE inhibitor development for hypertension in the 1960s (bradykinin-potentiating peptides from Brazilian arrowhead viper, Bothrops jararaca, venom) and latterly, for insulin-releasing peptide development for Type-2 diabetes (exendins from the venom of the American Gila monster, Heloderma suspectum [3]. They are not trivial human diseases. Cone shell venoms contain many components that act upon ion channels of cells, some of which are potent analgesics. Scorpion venoms likewise contain a multitude of ion channel toxins and one of them, chlorotoxin, is being assessed for its efficacy in treating brain tumours, notably malignant gliomas. Chlorotoxin binds to a multitude of chloride channels expressed by these tumour cells, but also inhibits the action and expression of the tissue matrix-degrading protease, MMP-2 [3]. However, little focused research for anticancer drug discovery has been carried out on the skin venoms of amphibians.

For most frog and some toad species, skin venoms contain a plethora of peptides that are targeted to molecular binding sites on the cells and tissues of predators. In most instances, they are active on targets in mammals, including human cells. These molecular targets are often specific receptors that normally bind endogenous regulatory factors controlling many aspects of a cell's behaviour. This is why these natural molecules represent a most intriguing source for drug lead-discovery that for the most part remains unexplored. There are ~4,700 known species of frogs and, on average, each produces 100 different peptides. This represents a total of nearly half a million molecules, of which probably < 1% have been structurally and functionally characterised. Of those that are known, anticancer activity has been noted for a considerable number that fall into 5 major categories: cytolysins, protease inhibitors, anti-angiogenics, immune system activators and neuropeptides [4-6].

Cytolysins were originally identified and called antimicrobial peptides (AMPs) due to their broad-spectrum of activity on microorganisms killed by destruction of their cell membranes. Although some were non-selective in their effects, killing mammalian cells as effectively as microbial cells, many were considerably more selective for the latter. The reason(s) for this differential effect is due to differences in membrane composition in microbial (prokaryotic) and mammalian (eukaryotic) cells. The membrane lipid composition of microbes produces a more negatively-charged membrane surface to which the amphibian cytolysins can readily attach. Their lack of membrane-stabilising cholesterol renders them more vulnerable to subsequent destruction. Cancer cells generally have altered membrane lipid compositions compared to normal cells, which involve both an increase in surface negative charge and a reduction in cholesterol. They have greater membrane surface areas than most normal cells due to an increase in the number of microvilli. These factors together render cancer cells a more vulnerable target for the actions of cytolysins thereby providing a higher degree of specificity. Although membrane disruption appears to be the main mechanism by which cytolytic peptides kill cancer cells, there is increasing evidence that other mechanisms are involved. Other targets for the anticancer actions of these peptides include nucleic acids and mitochondria, as well as activation of apoptosis. Although these targets are within the cell, the peptides gain entry through membrane interactions that ensure maintenance of specific targeting of cancer cells. Many analogues of natural amphibian skin cytolytic peptides are being designed with enhanced specificity and potency as anticancer agents [7,8].

Protease inhibitors and their target proteins, the proteases, are ubiquitous in Nature and both play fundamental roles in many life processes. They are of particular importance, as is the balance of their respective actions, in tissue growth, differentiation and repair, all of which are highly-regulated processes. Their deregulation is a characteristic feature of cancer and, not unexpectedly, proteases and their inhibitors are intimately involved. Aberrant protease expression, usually involving up-regulation or more commonly, ectopic expression, is not just a common finding in cancers, but may be central to their aggressive behaviour, such as invasion and metastasis. Matrix metalloproteases (MMPs), are largely responsible for degradation of the matrix proteins of connective tissues that surround cancers, thus permitting growth and directional invasion [9]. In cancers such as malignant gliomas the ectopic expression of MMP-2 facilitates invasion of surrounding neural tissues

leading to poor prognosis. Protease inhibitors could potentially represent a formidable class of anticancer drug and there is indeed increasing evidence to suggest this is the case. The presence of representatives of virtually every major class of protease inhibitor in the venoms of amphibians is most probably related to their regulatory roles in ordered tissue repair, a central aspect of which is the control of cell migration. With this in mind, their selection for this purpose renders them highly-appropriate lead compounds for designing inhibitor drugs for this therapy. A protease inhibitor-enriched preparation of soybeans has anticancer properties and the major proteins belong to a class of protease inhibitor named after its discoverers, Bowman and Birk. Such inhibitors (BBIs) are found solely in nature within the seeds of leguminous plants and grasses [10]. However, BBIs occur widely in amphibian skin venoms and their potencies and target proteases are very similar to their plant counterparts, but they are much smaller in molecular size, permitting deeper tissue penetration [11]. Synthetic replicates of these inhibitors have selective and are potent growth inhibitors of human breast and prostate cancer cell lines. Not all cell lines tested were inhibited, which suggests a highly specific rather than general cytotoxicity, and currently the discrete target through which BBIs mediate this anticancer activity is being sought.

Cancers may arise from single mutated cells and can grow in tissues until their mass approaches several millimetres in diameter, after which needs neovascularisation to acquire to supply the oxygen and nutrients required to sustain growth. Angiogenesis is restricted in adult life to events such as wound repair, vascularisation of the uterine lining during the early menstrual cycle, and pathological events such as macular degeneration and cancer [12]. This illustrates several important points in the understanding of the fight against cancer. There are many common molecular features between normal bodily processes, such as embryogenesis and wound repair, that are appropriate at certain times and under certain circumstances, and those that are hijacked by cancers. Cancer-specific targets for drug development are needed to ensure the minimum of collateral damage to normal body tissues. Angiogenesis is a process that apparently fulfils both of these criteria and is a common feature of the majority of solid cancers. Drugs that interfere with angiogenesis might also be effective in arresting invasion and metastasis. So why have so few drugs been developed for this purpose despite several decades of investigation? Many have been tested, and some can be effective for short periods then fail, while others can be effective in the short term, but were too toxic for continued administration. The former situation is a common feature of anticancer drugs and the latter is a common feature of many natural product and synthetic drugs [13]. Amphibian skin venoms contain many peptide components that have potent anti-angiogenic properties, and these are not used biologically to deter predators, but rather are vital to the regulation of wound healing that is most likely to occur when a frog is attacked. Rapid and regulated skin repair and revascularisation is essential to the repair of the frog skin, a multifunctional organ playing pivotal roles in respiration and excretion. These lower vertebrates may hold the key lead peptides for the design of drugs that will be effective in inhibiting angiogenesis in human cancers. Several peptides of different molecular classes that are effective against several recently identified anti-angiogenic targets are in the process of being clinically evaluated after showing promise in animal models.

The immune system plays a pivotal role in both preventing infection by microorganisms and fighting infections when they take hold. It is difficult to ascertain how many early cancers are contained, at least for some time, by the immune system and any one that finally succumbs could be the exception. The immune system has two components, the innate and the acquired. The innate is the most ancient and shares many molecules found in other organisms. This is a relatively non-specific system in contrast to the

A giant monkey frog (Phyllomedusa bicolor) from the rainforests of South America. This species produces one of the most complex skin secretions/venoms of any amphibian, and is particularly rich in peptides with a vast range of pharmacological effects on human tissues and cells, including some with potent anticancer properties.

acquired response, whose products, the antibodies, rank among the most specifically-targeted proteins occurring in Nature. The skin venoms of amphibians contain many groups of peptides that interact with and activate various cellular elements of the innate immune system. These actions include histamine release from mast cells, induction of leucocyte chemotaxis and potent adjuvant effects in eliciting acquired immune responses [14]. Several classes of these peptides, due to their potent immunostimulatory effects, could have potential applications in the treatment of cancer by either general stimulation of the immune system in cancer patients or by their specific interactions with cancer cells in a manner similar to the cytolysins. One such novel peptide containing 9 amino acids proved to be a most potent cytotoxic agent to a wide range of cancer cell lines in high-throughput screening, but was devoid of activity against microbes. Systematic investigation of this peptide is ongoing.

A major class of bioactive peptides in amphibian skin venoms are neuropeptide analogues. These occur in high diversity, but are often specific for certain amphibian families. These are of considerable interest to molecular bologists as they are structurally and functionally similar to neuropeptides found in mammalian (human) central and peripheral nervous systems. However, often the small structural differences serve to dramatically increase both their potency and stability. Bombesin is one such amphibian skin structural analogue of an endogenous human peptide, and this peptide is a potent mitogen for small cell lung cancer cells. Subsequently, not only did the cancer cells have receptors for the endogenous peptide through which amphibian bombesin acted, but cells themselves produced the endogenous peptide [15,16]. This phenomenon was one of the first examples of autocrine secretion, where cells have growth factor receptors but produce the growth factors themselves. Autocrine stimulation is a well-established phenomenon but is not in itself a good prognostic indicator for cancer cells. Most cancer cells will express specific neuropeptide

receptors, and in most instances their roles in tumourogenesis are not well-established or indeed, understood. A novel tachykinin peptide from amphibian skin that activates its receptors is a potent inhibitor of proliferation of selected human cancer cell lines [17]. This is the first example of a neuropeptide analogue from this source that displays such an activity, and has become the subject of intensive investigation to determine its mechanisms of action.

To summarise, while animal venoms in general are one of the most fruitful resources in terms of drug discovery, there has been little in the way of systematic effort in assessing the value of amphibian skin venoms as anticancer drugs. The small number of species that have been sampled and studied have produced novel molecules of many structural classes and modes of action. It is anticipated that some of these will soon progress to human clinical trials. ■

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Meet the Editorial Team

Pediatric Teratomas: Outcome Analysis

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Abstract

We have analysed the outcome of teratomas of all grades affecting various sites, and looked at factors influencing the outcome. A retrospective analysis on all children presenting with teratomas has been carried at a tertiary care centre in India. Data were retrieved from files and case papers from January 2004 to December 2012. The follow-up period was six months to eight years.

Forty-six children with teratomas were included (15 boys and 31 girls), of whom 29/46 were sacrococcygeal teratomas (SCT). Others were retroperitoneal teratomas (RPT; 7/46, ovarian teratomas (6/46), testicular teratomas (2/46), and one each of mesenteric and thymic teratoma. The age of the patients varied from 0 to 12 years. Alpha-fetoprotein (AFP) was raised in 34/39 patients; 41/46 underwent surgical procedures with complete surgical excision in 33 cases. Four patients with SCT did not have coccyx removal, of which three recurred. Histopathology showed 25 mature teratomas (19 SCT), 10 intermediate (six SCT), and eight immature teratomas (three SCT, two RPT, one ovarian, one testicular, one mesenteric). Adjuvant chemotherapy, Bleomycin, Etoposide, Cisplatin (BEP) regime, was given to 12 patients. Tumour-free survival was seen in 33/46 (71%), 4/46 (8%) expired on therapy, six (13%) were lost to follow-up after partial treatment and three (6%) refused treatment.

Teratomas occur predominantly in girls, 67% in this study. Alpha-fetoprotein is a good tumour marker, although false negatives occurred in 12.8%. Sacrococcygeal teratoma has a favourable outcome with complete tumour and coccyx removal. Recurrence rate with non-removal of the coccyx was 75%. Wide margins in surgical excision (high orchidectomy) ensured good outcome for prepubertal testicular teratomas. Nearly 20% of the cases abandoned treatment, resulting in a poorer outcome.

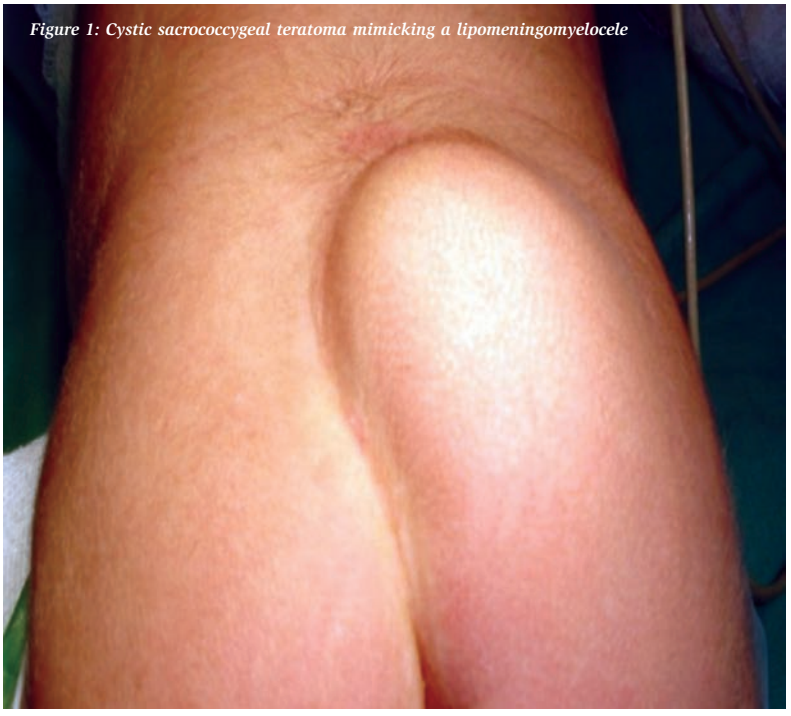

Figure 1: Cystic sacrococcygeal teratoma mimicking a lipomeningomyelocele

Introduction

Teratomas are common tumours in children, and even in infants, of which sacrococcygeal teratomas occur most frequently. The gonads are the most common sites, but teratomas can occur in any site of the body. Although most teratomas can be easily diagnosed and managed, there is a subgroup that behaves very aggressively, leading to higher morbidity and mortality. The maturity of the tumour indicates good prognosis; different grades of immaturity and malignancy change the clinical course of the disease and the prognosis significantly. The age, the site of occurrence of the tumour and its histopathology are interdependent factors that steer the course of the disease [1]. This report focuses on teratoma located in the gonads or in extragonadal locations (sacrococcygeal, retroperitoneal, mesenteric and thymic) in children from 0 to 12 years of age. Demographic details, treatment protocols, post-operative complications (especially recurrences) gave information contrary to that of developed countries. Since little data is available regarding outcome of children with teratomas from the developing countries and/or resource-challenged nations, the results are compared to those from developed countries.

Findings

Of the patients registered in the Pediatric Surgery and the Pediatric oncology department of Wadia Children's Hospital, a specialty tertiary care centre, 46 children had teratomas. Of these 15 were boys and 31 were girls (M:F ratio of 1:2). The majority of these children, i.e. 29/46 (63%) had sacrococcygeal teratomas (SCT).

Sacrococcygeal teratoma

Nine (31%) of the SCT were boys and 20 (69%) were girls. The age of presentation of both sexes is shown in Table 1.

Almost 83% of the children with sacrococcygeal teratomas had a solid mass on presentation and the remaining five presented with a cystic mass in the sacrococcygeal region (Figure 1), mimicking a lipomeningomyelocele. Altman's classification was used and pre-operative staging was done for the children with SCT; most of these tumours were either Stage 1 – 12/29 (41.3%) or Stage 2 – 11/29 (37.9%). About 10% had Stage 3 disease (Figure 2), whereas only 1/29 (3.4%) presented with Stage 4 SCT. Almost all the children with SCT – 27/29 were operated, two were not operated upon as one succumbed to pre-operative chemotherapy and the other is awaiting surgery post-chemotherapy. Of those who were operated upon, complete excision with coccyx removal was done in 20/27 (74%) children. Four children did not their coccyx removed as two of these four were operated elsewhere and the other two had cystic lesions, for whom diagnosis was established only post-operatively. Due to large masses at presentation, incomplete excision was

Table 1

No.	Age	Boys	Girls
1.	Newborn (<48 hours of birth)	1	4
2.	Neonate (<30 days of birth)	2	6
3.	Infant (<1 year after birth)	5	8
4.	1-3 years	1	2
	Totals	**9 (31%)**	**20 (69%)**

Table 2

S. no.	Surgical procedures	No. of patients	Details
1.	R0 resection with coccyx removal	20	
2.	Gross total resection without coccyx removal	4	2 – operated elsewhere 2 – cystic SCT
3.	Incomplete excision	3	Large mass, infiltrating surrounding structures
4.	Not operated	2	1 succumbed to chemotherapy, 1 awaiting surgery
	Total	**29**	

Table 3

Treatment	No. of patients	Histology	Chemotherapy	Outcome
Complete surgical excision (Figure 4)	4	Benign	-	TFS
Biopsy	2	1 –malignant teratoma 1 – endodermal sinus tumour		1-Abandoned 1-TFS
Denied	1			Abandoned

Table 4

Outcome	No. of patients (n=46)	%
Tumour free survival	33	71.7
Expired on therapy	4	8.6
Abandonment	9	19.5

done in 3/27 (11%) children. The surgical details of children with sacrococcygeal teratomas are given in Table 2.

About 10% (3/29) of children with SCT had recurrence. Non-excision of the coccyx was the cause of recurrence in all three. Two were operated elsewhere and in one the diagnosis of SCT was not established pre-operatively due to its cystic nature. Wide surgical excision of the recurrent lesions was done (Figure 3) and chemotherapy with BEP was given both preoperatively as well as postoperatively. Histopathology showed 19/29 (66%) had mature Grade 1 tumour, 6/29 (202%) had intermediate histology and only 10% (3/29) of SCT had immature histology. The outcome of children with SCT gave a five-year survival of 76%. Five patients (17%) abandoned treatment and two (7%) succumbed to chemotherapy.

Retroperitoneal teratoma

Seven children (15%) had retroperitoneal teratomas, presenting from the neonatal age group up to five years of age. Four were infants and three were in the post-infancy group. The ratio of boys to girls was 1:3. Alphafetoprotein was done in 5/7 children wherein high levels (> 1 lakh ng/ml) was seen in four and was normal in one child. The treatment details and the outcome are shown in Table 3.

Mesenteric teratoma – 2%

A one-year-old boy presented with a large solid cystic mass arising from the small bowel mesentry. Alpha-fetoprotein was 8 lakh units. An upfront surgery was done, and the mass excised; with residual tumour in situ, post-operative chemotherapy was given because the

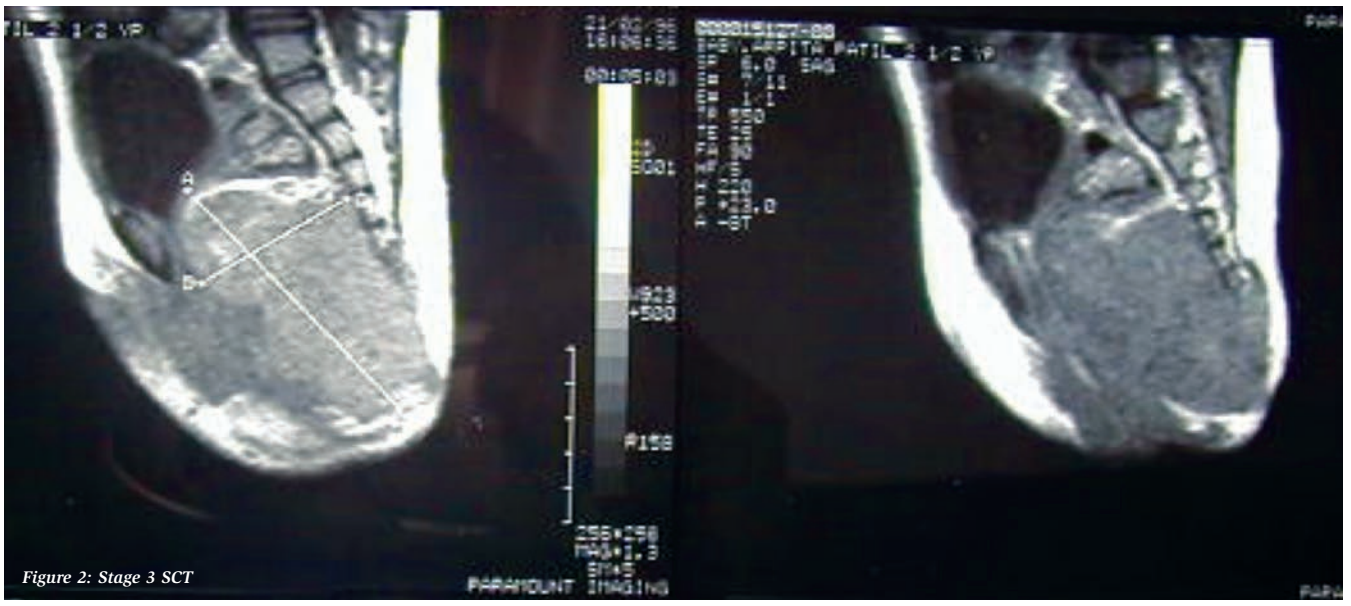

Figure 2: Stage 3 SCT

histopathology showed a malignant teratoma. Post-chemotherapy (five cycles of BEP) were given, and the child remains well without recurrence of the lesion after four years.

Thymic teratoma – 2%

A six-month-old boy presented with breathlessness, an xray of the chest showing widening of the superior mediastinum. CT-Scan of the chest showed a cystic mass in the superior mediastinum of about 7x5 cm. No tumour markers were measured. Upfront surgical excision of the cystic mass was carried out and the histopathology indicated a benign teratoma. The child is well and tumor-free after two years.

Gonadal teratomas – 17%

Two boys aged six months and three years with prepubertal testicular tumours underwent high orchidectomy. The former had high AFP pre-operatively (54,400 units) and histopathology showed an immature teratoma. In view of the normal AFP, no chemotherapy was given and the child was regularly assessed clinically as well as the AFP level. Follow-up for six years showed a healthy tumour-free child. The three year-old boy had a mature teratoma and is well one and a half years post-surgery with a normal AFP.

Six girls ranging from five to twelve years presented with ovarian masses (13% of all teratomas). Five of them underwent surgery, and one received pre-operative chemotherapy. One girl was denied treatment by her parents due to gender bias. Complete surgical excision (R0 resection) was done in four girls; but complete excision was not possible in one child, who was started on chemotherapy post-operatively, although the treatment was abandoned after two cycles and the parents took the child away against medical advice. Follow-up of four to eight years showed tumour-free survival of four girls (see Table 4).

Discussion

Most teratomas occur in girls, with an incidence of 67% in this series. Others (two to four) have noted a similar preponderance. The most common age of occurrence is usually in infancy (benign teratomas), although ovarian teratomas tend to occur in girls over five years of age. Similar to our findings, extragonadal tumours are known to occur in earlier life, i.e. in infancy, with the gonadal ones occurring in later life [2]. Sacrococcygeal teratoma is the most frequently occurring teratoma, which has a good prognosis [5], even with the presence of malignant components [6]. If treatment is given as per protocol and completed without any abandonment, tumour-free survival is unaffected by the size of the tumour or its histopathological characteristics. Recurrence can occur even when complete excision has been performed, but is unusual. The rate of recurrence of sacrococcygeal teratomas definitely increases if the coccyx is not excised or incompletely excised, as in three of the four children with non-excision of the coccyx.

For all types of teratomas, surgical intervention remains the main modality of treatment, with the occasional need for chemotherapy and other modalities [7]. Almost 90% of patients in our series underwent surgery, and only those abandoning therapy or succumbing to pre-operative chemotherapy did not receive surgery.

Mesenteries are very rare sites of occurrence. Despite tumours showing immature elements, the prognosis was good after complete excision. Very few cases of mesenteric teratomas have been reported in the literature, and malignant teratoma is even rarer [8,9].

The five-year free survival is as high as 92% for mature teratomas and up to 85% for immature teratomas [10], which can be achieved even in the developing countries when confounding factors are addressed. The rate of abandonment in our series was high (19%), being the main reason for poorer overall outcome compared to developed countries [11]. ■

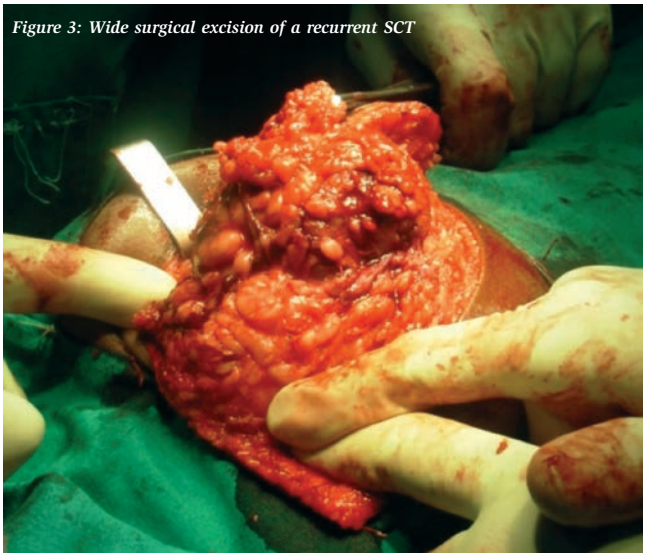

Figure 3: Wide surgical excision of a recurrent SCT

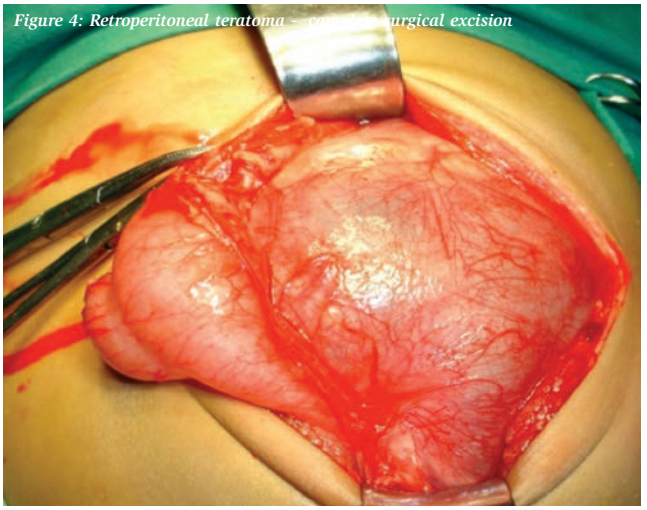

Figure 4: Retroperitoneal teratoma – complete surgical excision

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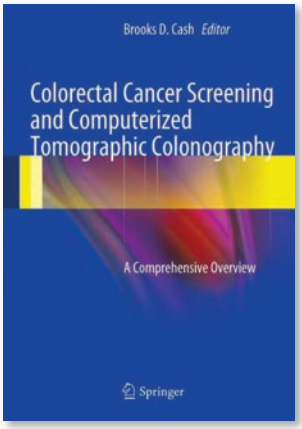
Book Reviews

Colorectal Cancer Screening and Computerised Tomographic Colonography – A Comprehensive Overview

Editors: Brooks D Cash. Published by: Springer New York. ISBN: 978-1-46145-942-2. Price: $189.00.



This multi-author work charts the development of computerised tomographic colonography (CTC), more commonly referred to as virtual colonoscopy, from the landmark presentation by Vining et al to the Society of Gastrointestinal Radiologists in 2004 to the present day. Early chapters cover the epidemiology and pathogenesis of colorectal cancer (particularly the adenoma-carcinoma sequence) an overview of screening techniques, the relevance of diminutive polyps and the difficulties of detecting flat and serrated adenomas. Subsequent authors explore the validation of CTC through multicentre trials from 2004-10 and its progressive ascendency over Barium enema, bowel preparation and imaging techniques, 2D versus 3D interpretation and limitations of CTC. The latter is particularly well covered, with copious full-colour illustrations of artifacts related to preparation, imaging and anatomical variants. A final chapter explores future directions for the technique including prepless colonic imaging using electronic (virtual) cleansing, virtual dissection (allowing the colon to be "opened up" and the mucosa examined in 3D) and computer-aided diagnosis.

Apart from two chapters all the authors are from the USA, and as a result some chapters have a somewhat commercial slant, with discussions of reimbursement and insurance coverage; economic considerations are nonetheless important and broadly applicable to the UK. Risks versus benefits of CTC are well covered: the average radiation dose per examination is currently around 5 mSv, roughly equivalent to a barium enema or an annual background dose. Ultra-low dose CTC has been trialled and shown to be effective in detecting polyps >10mm at a dose of 1.8-2.4 mSv, but adoption has been slow due to concerns over reduced image quality.

The book is beautifully illustrated and extensively referenced but, as is typical of multi-author works, can be a little repetitive. It will be of interest principally to radiologists and those responsible for planning screening programmes, but is also recommended to anyone with a primary interest in the diagnosis of colorectal cancer. ■

Richard Novell, Consultant Colorectal Surgeon, Royal Free London NHS Foundation Trust, London, UK.

Oxford American Mini-handbook of Cancer Supportive Care

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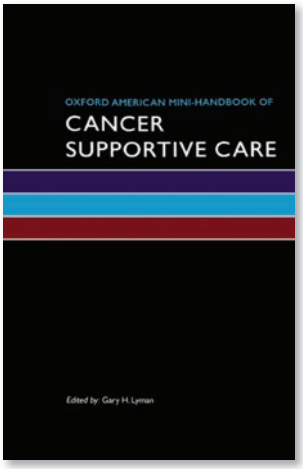

This relatively small, slim volume has been written by physicians from the Duke University Medical Centre, North Carolina. It is aimed at clinicians and other health care professionals who regularly care for cancer patients. Over 11 chapters, the subject matter ranges from symptoms that may be experienced by any oncology patient, including those receiving radical treatment, through oncological emergencies, to the management of the patient at the end of life. Where appropriate the aetiology, management and prognostic implications of each symptom are outlined.

Chapter one deals with fatigue and anaemia and includes indications for blood transfusion as well as quite extensive discussion around the use of erythropoiesis-stimulating agents. Other relevant medication and lifestyle adaptations are also discussed. Chapter 2 gives an excellent overview of febrile neutropenia, including risk factors, management and mortality rates. The next chapter (3) is on pain management, looking at the appropriate use of drugs and management of their side effects as well as non-pharmacological interventions. Chapter 4 deals in some detail with venous thromboembolism, with sections on risk factors, prophylaxis and treatment of existing thrombi. Chapter 5 looks at metabolic emergencies including electrolyte disturbance, renal failure and tumourlysis. Chapters 6, 7 and 8 cover paraneoplastic syndrome and oncological emergencies in the form of raised intracranial pressure, superior vena cava obstruction and spinal cord compression. In Chapter 9 the editor discusses the management of obstruction of the airway, gut and urinary tract as well as obstructive jaundice. An overview of the late effects of cancer treatment is given in Chapter 10. Finally, Chapter 11 covers care given in the period leading up to the end of life. This is a long chapter dealing with all aspects of care of both the patient and their carers and touching on some ethical issues such as those around the provision or withdrawal of nutrition and fluids. The book is well referenced and the index is comprehensive. Although it is written by physicians from the USA, on the whole it is relevant to practice in the UK. Overall, this is an excellent pocket reference book which would be useful for any health professionals, including general practitioners and allied heath professionals, who have contact with cancer patients. ■

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Recurrent Ovarian Teratoma with Glial Peritoneal Implant Eight Years After Original Surgical Resection


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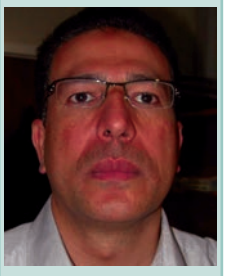
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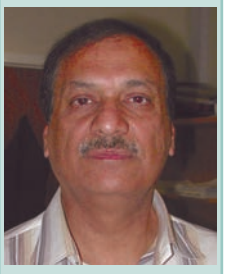
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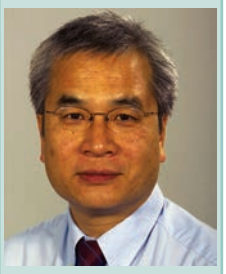
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Abstract

Immature teratomas are largely solid tumours that occur most frequently in the first and second decades. When associated with mature glial implants within the peritoneum, the prognosis is usually good, irrespective of the original tumour grade. However, there is no clear guidance as to how often and for how long these patients should be followed up, and there have been descriptions of cases of mature gliomatosis peritonei that have seemingly evolved into malignant tumours. We present a case of immature ovarian teratoma associated with mature glial peritoneal implants that was treated with surgery alone. The tumour recurred eight years later in the other ovary as a mature teratoma associated with mature glial peritoneal implants.

Introduction

Germ cell tumours constitute ~20% of ovarian neoplasms. Over 90% of these tumours are teratomas, which are derived from the three germ cell layers. While mature teratoma tends to be cystic and behave benignly, immature teratoma (that characteristically contains a mixture of adult/mature and embryonal/immature tissue mainly neuroepithelium) is usually solid and typically malignant [1].

Ovarian immature teratomas usually present in childhood or early adulthood with abdominal or pelvic pain, usually as a consequence of the effect of the tumour mass. This usually leads to investigation by imaging followed by a biopsy to confirm the histological diagnosis. Immatured teratomas may contain yolk-sac elements and secrete alpha-fetoprotein (AFP) and/or beta-HCG (human chorionadotrophin), which can be used as a marker of treatment efficacy and the detection of relapse. The treatment of choice for ovarian teratoma is complete surgical resection [1], which allows detailed histological examination regarding its malignant potential. This is may be followed by chemotherapy (either BEP or another platinum-based agent) dependent on the histological diagnosis and the staging [2,3]. Patients can expect 99% overall five-year survival for mature teratoma (92.2% event-free five-year survival) and 95.1% overall five-year survival (85.9% event free five-year survival) for malignant immature teratoma.

Prognosis of immature teratomas are related to size and stage of the tumour. The amount of immature tissue or microscopic grading is related to extraovarian spread [2]. When the teratoma is associated with gliomatosis peritonei (GP), the prognosis is usually better, irrespective of the original tumour grade [3,4]. However, malignant transformation of GP has been reported [1,5-7]. GP is a rare occurrence associated with solid ovarian teratoma, in which nodules composed of glial tissue are studded on the peritoneum, omentum and bowel wall. Although glial implants of GP are metastatic in nature, they occur with both immature and mature ovarian teratomas [8], and the peritoneal implants are mostly mature even when they originate from immature teratomas. Injury to the ovarian solid teratoma capsule may have a role in peritoneal implantation [4]. We report a case of immature ovarian teratoma associated with GP in a 14-year old girl who developed mature solid teratoma in the other ovary associated with GP after eight years of being well and without evidence of peritoneal disease.

Case report

A 14-year old Caucasian girl was seen by the Paediatric Services in Nottingham in December 2002, complaining of a two-week history of abdominal distension and vomiting. Examination revealed a large pelvic mass with mixed solid and cystic components extending 5cm above the umbilicus. Blood tests showed an elevated level of alpha fetoprotein (AFP, 111μg/L; normal level <10μg/L) and the tumour marker CA-125 (840kU/L; normal <60kU/L), whereas β-HCG and CEA were within the normal range. During laparotomy the left ovary had beenreplaced by a 20cm cystic/solid mass. The right ovary had a 1cm plaque of an indeterminate nature and there was no gross peritoneal/omental spread of disease. The patient underwent a left oopherectomy with right ovarian and peritoneal biopsy. Histology of the left ovarian mass showed immature teratoma with a wide variety of elements, including squamous and glandular epithelium, smooth muscle, fat, cartilage and bone. Abundant neural tissue was present, with foci of immature neuroepithelium sufficient to be regarded as a high grade (grade 3) tumour [2]. No yolk sac elements were found. The right ovarian plaque and peritoneal biopsy showed multiple glial microscopic deposits which, although predominantly of low cellularity, contained several foci of increasingly immature cellularity consistent with immature teratoma or gliomatosis peritonei. The consensus of opinion was that these foci were mmature teratoma rather than gliomatosis peritonei alone. Subsequent to surgical excision, the AFP and CA125 fell to the normal level within three weeks and have remained within normal limits to date.

The patient was considered suitable for a, 'watch and wait' programme of active surveillance without adjuvant chemotherapy. This was because the patient's tumour markers resolved to normal levels after the tumour was resected and this, therefore, represented a stage 1 tumour with complete removal of the malignant tissue. She remained under active surveillance for five years until 2007 when she was discharged from clinic.

In July 2010, the patient presented with a history of increasingly irregular periods over the previous nine

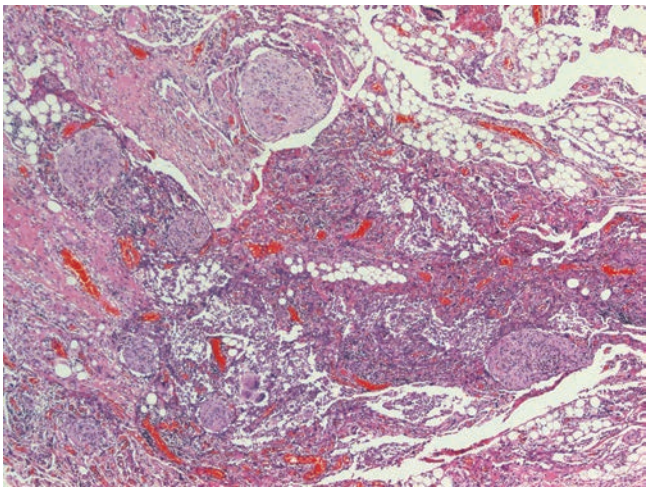

Figure 1: Ovarian immature teratoma with predominance of primitive neuroepithelial elements.

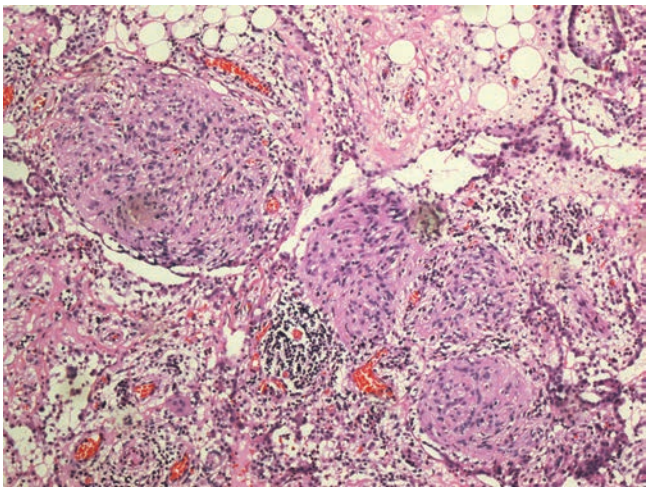

Figure 1B: Peritoneal implant of mature glial tissue secondary to the primary immature ovarian teratoma (Figure 1) and showing no evidence of immature elements, necrosis, nuclear atypia or abnormal mitotic activity. No epithelial elements present.

months associated with a brown vaginal mid-cycle discharge. A 48mm right adnexal complex mass was detected. All germ cell tumour markers remained within the normal limits. A staging CT scan of the chest, abdomen and pelvis confirmed a pelvic mass and located an isolated 2cm diameter serosal deposit on the liver surface. The patient underwent a laparotomy with right ovarian cystectomy and removal of a sub-diaphragmatic mass. Macroscopically, the right ovarian tumour contained hair and had the typical appearance of a mature cystic teratoma. The ovarian tumour had mature respiratory mucosa, skin and skin adnexa, and thyroid tissue with a focus of mature glial tissue. The histology of the sub-diaphragmatic mass also showed adnexal structures and ciliated epithelium. The final recommendation was to continue active monitoring, thus sparing the patient from the possibility of chemotherapy-induced infertility, with regular AFP measurement and yearly CT scans for the first two years. The patient remains well to date with normal menses and has no evidence of further recurrence of her teratoma. CA-125, AFP and β-HCG remain within normal limits.

Discussion

This is an unusual case of second primary mature cystic teratoma in the ovary associated with GP following a grade 3 immature solid teratoma in the other ovary with GP after eight-year history of complete recovery with no evidence of residual peritoneal disease. The patients did not receive chemotherapy, which is known to be associated with maturation of metastatic deposits of immature teratoma (chemotherapeutic retroconversion) [9]. The origin of GP remains controversial and its metastatic nature is widely accepted however, the occurrence of GP in association with mature solid teratomas questions the hypothesis of its metastatic nature. In the current case, GP occurred in association with mature cystic teratoma with the intact capsule. The ovarian teratoma was rich in mature glial tissue, but there was no evidence of peritoneal deposits following removal of the implants associated with initial immature teratoma of the left ovary. The possibility exists that the second mature cystic teratoma is a recurrence of the immature tumour in the other ovary, as supported by the presence of glial implants over the surface of the right ovary with the assumption of maturation of the recurrent teratomatous components of the right ovary. However, the synchronous recurrence of teratoma in the other ovary and glial tissue peritoneal implants in the upper abdomen after this long interval is a remote possibility. Therefore we believe that the diaphragmatic glial implants are most likely to be related to the right ovarian teratoma, despite being mature and cystic, and that the right ovarian teratoma is a second primary tumour rather than a recurrence of the primary tumour. Consistent with our observation, Gocht et al [8] reported the development of a mature teratoma associated with GP nine years following teratoma in the other ovary. However, the initial tumour was amature teratoma not associated with GP. Song et al [10] found that the overall recurrence rate after conservative treatment of mature teratoma was 2.5% after a mean period of eight years.

In our case, the raised AFP tumour marker associated with the first teratoma in 2002 would support the diagnosis of a malignant teratoma. The fact that the marker returned to a normal level after the left oopherectomy would suggest a stage 1a disease or at least the immature elements were contained within the surgically removed ovarian tissue. The adjuvant treatment of immature ovarian teratoma remains controversial, with little evidence to support the use of adjuvant chemotherapy post-surgery. Complete surgical resection gives an overall survival rate of 95.1%; as a result few patients undergo adjuvant chemotherapy, making its efficacy difficult to assess. Worse event-free survival has been noted with incomplete resection, higher stage, non-gonodal tumours, younger age and higher grade, the worse overall survival being noted for those with incomplete resection and higher grade.

Therefore the current recommendation is for close oncological follow-up with repeat AFP measurements to diagnose early relapse. In those who relapse, the decision to treat with adjuvant chemotherapy rests on the histological appearance of the tumour, with high grade immature teratomas most likely to require platinum based chemotherapy. ■

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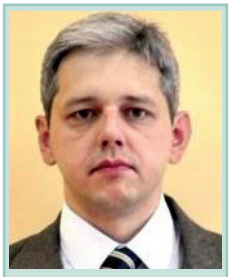
Neoadjuvant Chemoradiation Therapy in The Treatment Of Resectable Pancreatic Cancer



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Abstract
This article reviews currently used combinations of neoadjuvant chemoradiotherapy in the treatment of patients with resectable and borderline resectable pancreatic cancer, and discusses their advantages and disadvantages, and clinical results, with a special emphasis on the tolerability of a combined treatment employing preoperative radiation therapy in a hypofractionation regimen. Immediate, short- and long-term results of the management of patients with such tumours.

Introduction

Pancreatic cancer (PC) continues to be a virtually fatal disease even after radical surgery, in keeping with its extreme aggressiveness. Clinically identified 'early-stage' tumours can appear to be late-stage ones, as they are accompanied by multiple covert (clinically detectable) metastases in 33% of patients with resectable PC, but which can be detected immunocytochemically [1]. As a consequence, progression after apparently 'radical' surgery is the rule rather than an exception. This calls for a multimodality approach to treatment, the most common approach at present being that adjuvant chemotherapy (ACT) or concomitant chemoradiotherapy (CRT). There is no doubt that adjuvant therapy is necessary, but little consensus as to what the 'standard' should be. There is a geographic difference – whereas CRT is favoured in North America buttressed by the data from GITSC [2] and RTOG 97-04 [3], Europe opts for ACT proceeding from ESPAC-1 [4] and CONCO-001 [5] findings. The chief drawback of adjuvant CRT and CT is that 25-31% of patients do not receive the required adjuvant therapy in the event of post-operative complications, i.e. the treatment appears to be no more than palliative in nature [6].

Discussion

Unlike CRT and ACT, neoadjuvant CRT (NCRT) has no such drawbacks, yet its current application in the management of PC patients has not gained the same wide currency as the above methods.

The core of the neoadjuvant method is preoperative application of external beam radiation therapy (EBRT) used either on its own or concomitantly with chemotherapy. The benefits expected from applying it are:

1. Tumour restaging could avoid unnecessary laparotomies in patients with disease progression, despite CRT treatment. In other words, NCRT helps identify patients with a strong likelihood of a positive outcome, and also whether or not adjuvant therapy might be considered [7].
2. Reduction in the implantation of tumour cells released into the blood stream due to surgical intervention. As a result, NCRT lowers the incidence of loco-regional recurrence [3].
3. NCRT can be used to treat a large majority of patients.
4. From morphological studies, the degree of post-radiation pathomorphosis in response to the NCRT treatment points to its efficiency and also helps in the prognosis in each individual case [3].

Most authors report a good tolerance to NCRT treatment, and can reduce surgical complications, eg pancreatitis and pancreaticoenteroanastomosis failure following preoperative radiotherapy [3,8]. Furthermore, non-randomised studies show an increase in PC resectability to as high as 44-85% compared with outcomes without NCRT. There is also an improvement in median survival to 15-32 months [9,10] against 16-25 months for adjuvant CRT or CT treatment [4,11,12].

The use of preoperative CRT in an integrated PC treatment was first reported by Evans et al. [13]. Their study comprised 28 patients who received RT treatment at a total dose of 50.4Gy in 1.8Gy fractions in combination with long-duration CT infusions of 5-fluorouracil at 300 mg/m^2/day. The cases were restaged four to five weeks after the completion of the CRT treatment. Five patients had distant metastases, and 17 of the remaining 23 patients underwent resection. NCRT was well tolerated and this trial served as a stepping stone in promoting further investigations into neoadjuvant treatment strategies.

Modes of NCRT administration

The most wide-spread is *the classical fractionation regimen* both with and without induction CT [14,15]. This regimen is usually involves a total dose of 45-50Gy with 1.8Gy per fraction in combination with monochemotherapy of 5-fluorouracil at 300 mg/m^2/day for five days a week during the entire RT delivery period, followed by radical surgery three to four weeks after completion of the CRT treatment [16].

The classical fractionation regimen is commonly believed to have the following drawbacks:

- 1.8Gy is small and therefore insufficient to ensure maximum destruction of the cancer cell population of the pancreatic head;
- Possibilities of a continuous radiation therapy of the pancreatic head cancer at a total dose of 50-60Gy are limited by the level of tolerance of the surrounding normal organs and tissues, including liver, intestines, spleen, kidneys and bone marrow. Most patients are forced to discontinue radiation treatment for 10-12 days due early side effects. As a consequence, there is a need for increasing the total dose by 10–12% to achieve a desired therapeutic effect, which leads in a predominant number of cases to the emergence of serious side effects of III-IV degrees of severity in normal organs and tissues, and the required therapeutic dose delivery is still not achieved. For example, Breslin et al. [16] noted that with NCRT treatment, only 68% of patients go the full distance with chemoradiotherapy, whereas 27% of patients receive <75% of the planned dose.

Table 1: Results of administering split-course neoadjuvant CRT in the management of pancreatic cancer

Authors	Neoadjuvant therapy modes / number of patients involved	Resectablity	Median survival / all patients / months	Median survival / operated patients / months
Snady H. et al. [6]	EBRT (three split-courses of up to 54Gy at 2Gy per fraction, on days 1-5, days 8-12, days 29-33, days 36-40, and on day 56 – additional 14Gy in equal fractions with a total of 54Gy) + 300 mg/m^2 of streptozocin and 100 mg/m^2 of cisplatin; n=68	20/68 (29%)	23.6	32.3
Magnin V. et al. [17]	EBRT in two split-courses of 15Gy with a 2-week gap (n=10), or 45Gy in fractions of 1.8Gy (n=22) concurrently with cisplatin and 5-fluorouracil bolus infusion; n=32	19/32 (59%)	37.2% (2-year survival)	59.3% (2-year survival)
Adhoute X.et al. [18]	EBRT of 45Gy in 1.8Gy fractions (n=22) concurrently with cisplatin and 5-fluorouracil bolus infusion (with a split-course administered to six patients)	8/33 (24%)	16	–

Table 2. Results of administering hypofractionated neoadjuvant CRT in the management of resectable pancreatic cancer

Authors	Neoadjuvant therapy modes / number of patients involved	Resectablity	Median survival / all patients / months	Median survival / radically operated patients / months
Pisters P.W.T. et al. [19]	EBRT of 30 Gy with 3 Gy per fraction + 300 mg/m2/day of 5-fluoroucil 5 days per week; n=35	19/35 (71%)	12 months 14% (3-year survival)	19 months 28% (3-3-year survival)
Evans B.D. et al. [8]	EBRT of 30 Gy with 3 Gy per fraction concurrently with once-weekly monochemotherapy of 400 mg/m2 of gemcitabine (7 infusions). RT started 48-72 hours after the 1st gemcitabine infusion (10 fractions over two weeks)	73/86 (85%)	22.7 months 27% (5- year survival)	34 months 36% (5- year survival)
Small W. et al. [9]	EBRT of 36 Gy with 2.4 Gy per fraction concurrently with 1,000 mg/m2 of gemcitabine monochemotherapy. During cycles I and III, gemcitabine was delivered in the above dosage on days 1, 8 and 15 during a 21-day cycle. During cycle II, gemcitabine was administered on days 1, 8 and 15 of a 28-day cycle concurrently with conformal 3D RT.	17/39 (44%)	94% (1- year survival)	73% (1- year survival)
Varadhachary G.R. et al. [20]	EBRT of 30 Gy with 3 Gy per fraction concurrently with once-weekly monochemotherapy of 400 mg/m2 gemcitabine (a total of 7 infusions). RT started 48-72 hours after the 1st delivery of gemcitabine (10 fractions over 2 weeks). Prior to CT, once-biweekly administration of 750 mg/m2 gemcitabine plus 30 mg/m2 of cisplatin (a total of 4 infusions).	52/79 (66%)	18.7 months	31 months
Zimmermann F.B. et al. [10]	EBRT of 30 Gy with 3 Gy per fraction 5 days a week concurrently with monochemotherapy of 300 mg/m2/day of 5-fluorouracil 7 days a week. Patients with borderline resectable cancer underwent the same RT treatment plus 2 sessions of induction CT employing 75 mg/m2 of cisplatin and 1,250 mg/m2 of cisplatin.	9/17 (52.9%)	13 months 53% (1-year survival) 18% (2- year survival)	–
Katz M. H. G. et al. [21]	EBRT of 30 Gy with 3 Gy per fraction plus once-weekly 400 mg/m2 of gemcitabine during 7 weeks or once-biweekly 750 mg/m2 of gemcitabine and 30 mg/m2 of cisplatin (a total of 4 infusions)	119/176 (44%)	20 months	32 months

- The total time of concomitant chemoradiation treatment is quite lengthy (five to six weeks), thereby making it a laborious and costly procedure requiring a long hospital stay.
- The optimal RT dosage in the classical fractionation mode for treating the pancreatic head cancer is unknown.
- The need for a recovery period prior to surgery leads to its postponement.

The application of a *split-course regimen* carries the disadvantages of the classical fractionation mode described above. In addition, respite in RT administration results in the loss of local control of the cancer of up to 40-50% (see Table 1).

The *hypofractionation regimen* was devised to improve loco-regional cancer control, reducing the total treatment time and lowering the risks of side effects for the surrounding normal organs and tissues of the pancreas. To date, application of the hypofractionation regimen has given encouraging results (Table 2).

Table 2 shows that cancer resectability in the event of applying the hypofractionation regimen ranges from 44 to 85% against 23% achieved by employing NCRT in the classical regimen. Although enhancement of the classical regimen by employing induction CT helps to raise resectability to 29%, this falls far short of the hypofractionation results [22].

No less significant is the fact that the administration of NCRT (Tables 1 and 2) increases average median survival of patients compared with patients who underwent only adjuvant chemo- or chemo-radiation therapy.

One of the NCRT disadvantages both in the classical fractionation and hypofractionation modes is an increase in the length of the preoperative period [7], which may at first glance appear to have a negative effect on the treatment outcome. However, Varadhachary et al. [20] showed that the length of the preoperative period did not affect the resectability results. The study compared preoperative EBRT (30Gy with 3Gy per fraction) administered in combination with gemcitabine therapy with a regimen that combined EBRT (30Gy at 3Gy per fraction) with gemcitabine/cisplatin therapy. Despite a longer preoperative period in the latter case, no statistically significant differences were reported with regard to resectability, which was 68% for the gemcitabine + cisplatin regimen and 75% for the gemcitabine regimen ($p = 0.27$).

Conclusions

Proceeding from the above, there are grounds for claiming that, compared with adjuvant chemoradiation, neoadjuvant chemoradiation therapy increases resectability, and raises the survival median and overall survival times of patients with resectable or borderline resectable pancreatic cancer. Furthermore, application of the hypofractionation regimen produces better outcomes than NCRT administered in a classical fractionation regimen.

However, multicentre randomised trials are needed if we are to obtain conclusive data on the efficacy of neoadjuvant chemoradiation therapy, including that used in the hypofractionation mode. In the absence of such data, the positive effects of neoadjuvant CRT cannot be regarded as proven. ■

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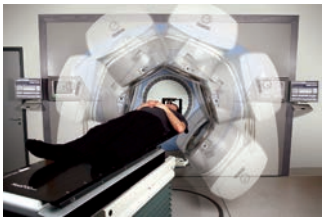
News update

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.

Elekta celebrates 10th anniversary of image guided radiation therapy



Elekta recently celebrated the 10th anniversary of the first clinical use of 3D Image Guided Radiation Therapy (IGRT) with the Elekta Synergy® system. The first commercial linear accelerator to bring 3D image guidance into the clinical workflow, Elekta Synergy combines soft issue imaging and treatment in a single system. Clinicians had at last attained the ability to visualise the treatment target, improving radiation therapy for cancer patients.

Elekta Synergy Research Group defines IGRT history

Elekta Synergy and IGRT development began in 1997 with William Beaumont Hospital, USA), with other world-class centres joining later to form the IGRT consortium. These included The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital (NKI-AVL, Amsterdam, The Netherlands), Princess Margaret Hospital (Toronto, Canada), The Christie Hospital (Manchester, UK), Thomas Jefferson University (Philadelphia, Pa., USA) and University Hospital of Würzburg (Würzburg, Germany). The collaboration with Elekta and this research group led to the creation of protocols driven by real-life clinical experience and a suite of software tools designed to support efficient workflow in today's busy clinic.

For further information contact:
Patrick Greally, Elekta Limited,
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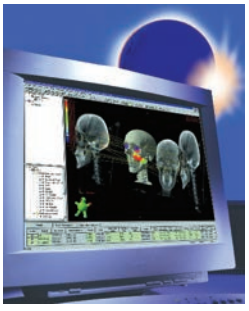
XVI 5.0 is not available for sale or distribution in all markets. Please contact your local representative for more details.

Varian's Eclipse System integrates with Elekta Machines for VMAT treatments



Varian's Eclipse treatment planning system.

Varian Medical Systems has successfully integrated its Eclipse™ treatment planning system with Elekta linear accelerators to deliver VMAT treatments at Kantonsspital St Gallen in Switzerland. An 83-year-old patient with non-Hodgkin's lymphoma has become the first patient in the world to be treated using this combination of software and equipment.

"We have been using Eclipse to plan other types of radiotherapy treatments for many years and have very good experience delivering those treatments on our Elekta treatment machines," says Dr Ludwig Plasswilm, the hospital's chief of radiation oncology. "We wanted to introduce faster volumetric modulated arc treatments in order to serve more patients more effectively.

"Physicists at our department worked on the development of this new approach with Varian, which has demonstrated its commitment to open architecture for clinical systems, and we have now seen successful integration of Eclipse with our treatment machines," said Dr Plasswilm. "We have now initiated more advanced volumetric treatments and our experience so far is that the integration is very good with a natural workflow."

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Introducing the Paxman Hair & Scalp Care Range

Paxman, the leading the leading global expert in scalp cooling has recently launched a hair and scalp care range specially developed with the specific hair and scalp needs of those using scalp cooling in conjunction with chemotherapy treatment.

The uniquely formulated gentle products are available to everyone, especially benefiting those with sensitive skin and allergies and also patients undergoing chemotherapy treatment. All products are dermatologically tested, safe, thoroughly researched and use raw ingredients which represent the very latest development in hair and scalp treatment.

Paxman are delighted to be working in collaboration with leading consultant Trichologist, Iain Sallis, who has assisted in giving his expert advice for patients in how to best care for their hair when using scalp cooling with chemotherapy treatment.

As a family business borne out of the Chairman's wife losing her hair whilst receiving chemotherapy for breast cancer, Paxman know first-hand that this is often devastating. We also know that the fear of hair loss has even been known to cause refusal of treatment by 8% of applicable patients.

For more information about Paxman haircare please visit paxmanhaircare.com or call +44 (0)1484 349444.

Swiss cancer centre delivers higher doses to treat patients

Clinicians at a leading cancer centre in Switzerland have commenced advanced lung and liver radiotherapy treatments by delivering higher doses using a Varian Clinac® medical linear accelerator. Flattening filter free (FFF) treatments which enable fast dose delivery capabilities are allowing doctors at Genolier Clinic to shorten treatment times and deliver stereotactic body radiotherapy and stereotactic radiosurgery for hard to treat tumours.

"Irradiation time is critically important for patients because shortening the time taken to deliver the dose may help to significantly improve the level of patient comfort," says Dr Jacques Bernier, head of radiation oncology at Genolier Clinic. "Through using such FFF treatments and delivering the beam faster, we also see greater precision as there is less opportunity for patient motion. Our objective is always to treat patients with maximum precision and in the best conditions possible for them."

Dr Bernier says faster treatment times also mean greater throughput, as each linear accelerator is able to treat more patients each day. "This helps us to avoid long waiting lists of patients as demand for cancer treatments increase," says Dr Bernier.

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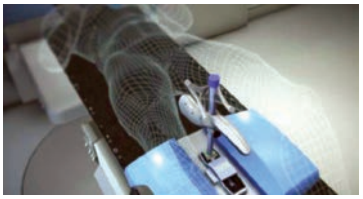
Elekta receives CE marking for Clarity 4D Monitoring



Elekta has received CE marking for its Clarity® 4D Monitoring system permitting European clinics to implement this new way of reducing the uncertainty caused by prostate motion during radiation treatment. Physicians will be able to monitor the motion of the prostate with sub millimeter accuracy during the delivery of therapeutic radiation beams.

The ability to continuously visualise the prostate and surrounding anatomy during treatment is especially important for clinicians pursuing advanced prostate protocols, such as reduced margin hypofractionated therapy or advanced stereotactic ablative body radiotherapy.

Continuous target visualisation

4D monitoring of the prostate with Clarity during treatment offers continuous tracking of the target and imaging of the surrounding anatomy, including the bladder, rectum and penile bulb. Clinicians are keen to avoid this surrounding anatomy to minimise the chance of side effects of treatment such as erectile dysfunction, incontinence or rectal bleeding. Being able to visualise these structures during treatment could potentially enable clinicians to create plans with tighter margins around intended targets, thereby minimising radiation exposure to healthy tissue.

Clarity 4D Monitoring uses Autoscan acquisition technology to robotically acquire live transperineal ultrasound images of soft tissue anatomy. This comfortable, non-invasive imaging procedure does not involve any extra radiation dose to the patient and does not require the use of implanted markers.

Learn more at www.elekta.com/clarity.

Major technology evolution set for Medipass Mes in Leeds

Medipass Healthcare, a leading provider of Managed Equipment Services (MES), announced this week that two of the recently launched Versa HD™ radiotherapy systems from Elekta will be installed as part of its MES in Leeds, making the Leeds Cancer Centre a world reference site for this innovative technology.

Cancer patients referred to the £220M Leeds Cancer Centre, situated on the campus of St James's University Hospital, will soon benefit from the streamlined acquisition within the Medipass MES of one of the most advanced linear accelerators in the world. Versa HD, featuring a revolutionary combination of speed and accuracy, is designed to improve patient care and treat a broader spectrum of cancers. It is expected that the radiotherapy department at the Leeds Cancer Centre will begin treating patients on Versa HD this July.

The Managed Equipment Service in Leeds is provided by Medipass Healthcare to the Leeds Teaching Hospitals Trust as part of a 15-year equipment concession in partnership with the project company St James's Oncology SPC Ltd. Stewart MacDuff, Manager of the Medipass MES in Leeds said, "This groundbreaking installation was only possible because we have such a close working relationship between Medipass and our project partners – St James's Oncology SPC Ltd, the Leeds Teaching Hospitals Trust, and Elekta."

For more information contact Sophie Seymour T: +44 (0)7881 906407.

Addenbrooke's Hospital Increases Access to the Latest Radiation Treatment for Prostate Cancer

According to Cancer Research UK, prostate cancer is the most common malignancy in men, and in the United Kingdom, approximately 40,000 cases are diagnosed annually. At Addenbrooke's Hospital, more prostate cancer patients are receiving a rapid form of Intensity Modulated Radiation Therapy (IMRT) called Volumetric Modulated Arc Therapy (VMAT). This is due to the centre's integration of advanced beam-shaping technology and VMAT software in two Elekta treatment machines that the center acquired in 2011 and 2012. VMAT enables the radiation dose to conform more precisely to the tumour shape by modulating the beam as it rotates round the patient.

With VMAT, single or multiple radiation beams sweep in fast, uninterrupted arcs around the patient. VMAT's high-speed IMRT delivery is best exploited with high-speed beam shaping, a benefit that Elekta's Agility™ 160-leaf multileaf collimator (MLC) provides.

Addenbrooke's was able to upgrade its current systems by purchasing the new MLC and VMAT option to offer advanced radiation delivery to their patients. The clinic began treating prostate cancer patients in March 2013.

"These Elekta machines are increasing the numbers of prostate cancer patients in our department that can benefit by having IMRT." says Simon Thomas, head of radiotherapy physics at Addenbrooke's.

For further information contact: Patrick Greally, Elekta Limited, T: +44 (0)1293 654 462, E: Patrick.Greally@elekta.com

Brain cancer treatments lag seriously behind

A new report released earlier this year by Brain Tumour Research shows that treatments for brain tumours lag seriously behind other cancers. This report also shows that spending for brain tumour research is falling while both new instances of brain tumours and mortality rates from the disease are both on the rise.

Brain cancer is the biggest cancer killer of the under 40s and responsible for over 20 years of life lost in the average patient, making this the most lethal cancer by this measure. Brain Tumour Research is campaigning for a sea-change in the research funding priority and calling for government to extend the reach of the national cancer register to include all research grants and research on cancer across the UK.

Sue Farrington-Smith, Chief Executive of Brain Tumour Research, said: "Lives are being devastated; people are living without hope. Action is needed now – by the government, the larger cancer charities and the public. Please help raise awareness of and support the research. We can't afford to wait."

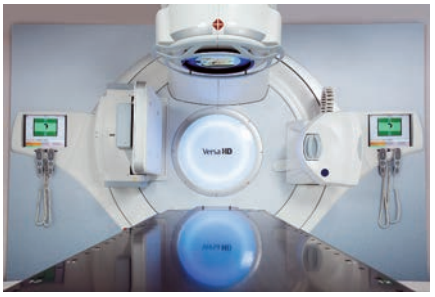
Professor Geoff Pilkington, Neuro-oncologist at the University of Portsmouth added: "Talented young graduates are being driven to other research areas where the funding is historically more robust."

Find out more: www.braintumourresearch.org/published-reports

Elekta's Versa HD System Now Features Automated Breath Hold Gating for Improved Breast and Lung Radiotherapy

Users of Elekta's Versa HD™ linear accelerator can now bring target immobilisation to new levels through automated gating with Active Breathing Coordinator™. For anatomies affected by respiratory motion, Active Breathing Coordinator provides non-invasive, internal immobilisation of the target, triggering radiation delivery when anatomy is immobilised.

Automated gating with Active Breathing Coordinator recently received CE marking from the European Union, and in combination with Elekta's Response™ gating interface, provides additional benefits to both the Versa HD clinically-tailored solutions for treating breast and lung cancers.



Active Breathing Coordinator helps patients pause their breathing at a precisely indicated tidal volume – a deep-inspiration breath-hold – which increases the distance between the tumour and critical structures, resulting in the ability to reduce doses to the critical structures.

By consistently immobilising the target in an identifiable, repeatable and stationary position, clinicians are better able to reduce tumour margins and implement dose escalation and hypofractionation strategies, such as SBRT. Automated beam delivery increases clinical confidence and efficiency, in addition to reducing treatment times over manual techniques.

Versa HD and Active Breathing Coordinator with automated gating are not available for sale in all markets.

For further information contact:
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Single injection may revolutionise melanoma treatment, Moffitt Study shows

A new study at Moffitt Cancer Center could offer hope to people with melanoma, the deadliest form of skin cancer. Researchers are investigating whether an injectable known as PV-10 can shrink tumours and reduce the spread of cancer. PV-10 is a solution developed from Rose Bengal, a water-soluble dye commonly used to stain damaged cells in the eye. Early clinical trials show PV-10 can boost immune response in melanoma tumours, as well as the blood stream.

"Various injection therapies for melanoma have been examined over the past 40 years, but few have shown the promising results we are seeing with PV-10," said Shari Pilon-Thomas, Ph.D., assistant member of Moffitt's Immunology Program.

In the initial study, researchers injected a single dose of PV-10 into mice with melanoma. The result was a significant reduction in the skin cancer lesions, as well as a sizable reduction in melanoma tumours that had spread to the lungs. The researchers said the dye solution appeared to produce a robust anti-tumour immune response and may be safer than existing immunological agents.

For further information visit:
http://www.pvct.com

Cancer Patients in Lebanon Treated on Country's First TrueBeam Radiotherapy and Radiosurgery System

Cancer patients in Lebanon have gained access to fast and precise radiotherapy and radiosurgery treatments with the clinical deployment of the country's first Varian TrueBeam™ medical linear accelerator. A 24-year-old man with sino-nasal cancer was the first person in Lebanon to be treated on the newly-installed TrueBeam system at the Hotel-Dieu de France Hospital (HDF) of the University of St Joseph in Beirut.

The patient received RapidArc® volumetric modulated arc therapy (VMAT) to help spare the parotid glands from exposure during treatment. "We were able to deliver his treatment in just two continuous arcs or rotations of the machine rather than having to stop and start the machine to deliver the treatment beam from different angles," said Dr. Elie Nasr, professor and chairman of HDF. "The integrated imaging enabled us to carefully align the patient every day and showed us the progress of the

treatment as we saw the tumour shrinking over the course of treatment. By sharing this information with the patient we are able to reassure them and increase their commitment to the treatment."

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The Christie Hospital NHS Foundation Trust awards OIS a three year contract for the provision of immobilisation devices

After an extensive review across all three Christie Hospital sites, Oncology Imaging Systems Ltd (OIS) are delighted to have been chosen as the exclusive supplier for all thermoplastic materials to the trust.

This contract is to last for three years with a possible extension for an extra year and starts with immediate effect.

Lead Radiographer, Pat Lawrence said "Our aim is to standardise the use of thermoplastic material across all of The Christie's three sites and following a full evaluation we are delighted to choose OIS as our main supplier. The contract between ourselves and OIS further strengthens our ongoing working relationship and gives us confidence to provide the best possible patient care."

The thermoplastic can be used in conjunction with the kVue couches and Pentafix inserts, also supplied by OIS, meaning overlay boards are no longer necessary for most treatments, which in turn reduces skin dose to the patients.

Managing Director of OIS, Steve Imber commented "This contract is another significant achievement for OIS and we are delighted to be working with one of the world's leading cancer centres."

For further information
T: +44 (0)1825 840 633,
E: sales@oncologyimaging.com or
visit: www.oncologyimaging.com

Journal Reviews

Clinical Breast Cancer

Prognostic clinico-pathological factors on multivariate analysis following preoperative systemic chemotherapy for triple negative breast cancers

Asaga S, Kinoshita T, Hojo T, Suzuki J, Jimbo K, Tsuda H. Clinical Breast Cancer 2013 Feb;13(1):40-6.

This is a retrospective follow up study aimed to identify significant prognostic factors for triple negative breast cancer (TNBC) patients receiving preoperative systemic chemotherapy (PST). A total of 135 triple negative breast cancer patients amongst the 4195 operable primary breast cancer patients were analysed for significant prognostic factors among different clinical and pathological variables. Kaplan-Meier curves and Cox proportional hazard modelling statistical tests were used in a univariate and multivariate analysis for disease-free survival (DFS) and overall survival (OS). Among the 135 triple-negative breast cancer patients, the median patient age was recorded at 54 years, median tumour diameter on palpation was found to be 4.5 cm, and there were 62 patients who had clinically node positive disease. Following anthracycline-taxane (Epirubicin, Doxorubicin, Cyclophosphamide and Paclitaxel) chemotherapy in concurrent (up to 2002), sequential and isolation regimens; the clinical response and pathologic complete response rates recorded was 76% (103 patients) and 21% (29 patients) respectively. Median disease-free survival was found to be 44.4 months and median overall survival 49.2 months. Univariate and multivariate analysis showed that that completion of chemotherapy, better clinical response, fewer positive nodes, and lower histologic grades were significant factors associated with both disease-free and overall survival.

Reviewer's opinion: This is a small retrospective study aimed at analysing other clinico-pathological factors (besides the pathological complete response; pCR) as prognostic markers in TNBC subtype following preoperative systemic chemotherapy in Japanese population. Previous studies have shown pCR following PST as an independent prognostic marker across all breast cancer subtype including TNBC. However, it is well known that TNBC subtype tends to develop visceral metastasis and show aggressive phenotype despite high pCR rates. This study therefore, assessed other clinico-pathological variables such as completion of PST, clinical response, T and N status, lymphatic and vascular invasion, and histological grade alongside pCR for DFS and OS in a multivariate analysis. Interestingly the findings from this study showed completion of PST and clinical response and not pCR as strong surrogate markers of favourable prognosis. Further, TNBC patients with a family history of breast cancer were found to have similar prognosis to patients with sporadic disease with the phenotype. This study is first to assess the role of pCR as independent prognostic marker with anthracycline-taxane primary systemic chemotherapy focused on TNBC subtype. The study findings challenge the status of pCR as independent prognostic factor the TNBC subtype; it provides researchers a much food for thought to consider the role of clinical response as a prognostic marker in the TNBC phenotype in larger studies. – TH

Alteration of HER2/neu status following neoadjuvant chemotherapy in invasive breast cancer

Influence of neoadjuvant chemotherapy on HER2/neu status in invasive breast cancer. Li P, Liu T, Wang Y, Shao S, Zhang W, Lv Y, Yi J, Wang Z. Clinical Breast Cancer 2013 Feb;13(1):53-60.

The study evaluates HER2/neu status of invasive breast cancers on core biopsies and surgical resections following neoadjuvant chemotherapy treatments (NACT). Reliably estimating HER2/neu expression in breast cancer is important for predicting patient prognosis and optimising adjuvant therapeutic strategies. A total of 131 patients with primary breast cancer treated with anthracycline-and/or taxane-based NACT were evaluated by immunohistochemical (IHC) study for HER2/neu status on core needle biopsies before NACT and residual breast cancers surgical resection specimens or-positive axillary lymph nodes post-NACT. Thirty-two pairs of specimens with discordant HER2/neu IHC scores were analysed by fluorescence in situ hybridisation (FISH). After NAC, 23.4% (29 of 124) of tumours showed down regulated HER2/neu expression by IHC. Alterations of HER2/neu IHC scores did not significantly correlate with tumour subtype, pathologic response to NACT, adjuvant regimen, or time interval from the last chemotherapy to surgery. HER2/neu protein overexpression level was associated with favourable pathologic response to anthracycline and taxane-based chemotherapy. However, tumours with altered HER2/neu IHC scores after NACT revealed stable HER2/neu gene amplification/nonamplification by FISH analysis. In conclusion, NACT for breast cancers resulted in the alteration of HER2/neu status by IHC, but tumours were found to have stable gene amplification status by FISH. However, HER2/neu protein overexpression indicated greater sensitivity to neoadjuvant anthracycline- and taxane-based chemotherapy. Thus, retesting HER2/neu IHC status in residual tumours after NACT is recommended in order to optimise adjuvant systemic therapy.

Reviewer's opinion: This study compares the HER2/neu expressions in pre-treatment core biopsy and post-treatment resection specimens containing residual tumour following anthracycline-taxane chemotherapy. The aim was to identify alteration in the HER2/neu receptor status following NACT affecting the decisions to offer adjuvant anti-HER2/neu targeted treatments. The study makes a valid case for assessing HER2/neu status post-NACT as statistically significant changes in ER/PR expression and Ki-67 labeling index after administration of NACT have been identified but the influence of NACT on HER2/neu status however, has not been adequately investigated. The study findings of HER2/neu status affected (down regulated) by NACT might have important clinical consequences for adjuvant systemic treatment and therapy optimisation post surgery. However, the discordance seen on IHC between the pre and post –NACT specimens even though could be related to intratumour heterogeneity, sampling error and technical variability; the influence of these factors in previous studies has been found to minor. Hence, the role of therapeutic agents in down regulation of receptor status assumes a much greater importance. – TH

Neuro-Oncology

Metabolic response of glioma to dichloroacetate measured in vivo by hyperpolarised 13C magnetic resonance spectroscopic imaging

Park JM, Recht LD, Josan S, Merchant M, Jang T, Yen YF, Hurd RE, Spielman DM, Mayer D. Neuro-Oncology 2013;15(4):433-41.

Normal tissues obtain the bulk of energy needs via oxidative phosphorylation (OXPHOS) of multiple energy substrates; solid tumours, including glioma, derive a disproportionate amount of energy via glycolysis, even when oxygen tension levels are high, a phenomenon known as the Warburg effect. This metabolic phenotype of glioma leads to elevated lactate labeling in metabolic imaging using hyperpolarised [1-13C]pyruvate. Although the pyruvate dehydrogenase (PDH)–mediated flux from pyruvate to acetyl coenzyme A can be indirectly measured through the detection of carbon-13 (13C)-labeled bicarbonate, it has proved difficult to visualise 13C-bicarbonate at high enough levels from injected [1-13C]pyruvate for quantitative analysis in brain. In the present study, an optimised protocol for chemical shift imaging and high concentration of hyperpolarised [1-13C]pyruvate were used to improve measurements of lactate and bicarbonate in glioma-transplanted rat brains. Metabolite ratios of lactate to bicarbonate were calculated to provide improved metrics for characterising tumour metabolism. The results showed that glioma and normal brain were well differentiated by lactate-to-bicarbonate ratio, and a stronger response to dichloroacetate (DCA) was observed in glioma than in normal brain. This study suggests that the simultaneous detection of lactate and bicarbonate provides a tool for a more

comprehensive analysis of glioma metabolism and the assessment of metabolic agents as anti-brain cancer drugs.

Reviewer's opinion: Since altered metabolism is a newly recognised hallmark of cancer cells, novel anti-cancer therapies are currently under development aiming to control tumour growth by reversing the Warburg effect. Glioblastoma multiforme is one of the most aggressive cancers and there is a need for methods to assess the effects of therapy acutely after administration, particularly treatments involving metabolic modulation. This study demonstrates for the first time the feasibility of quantitatively detecting 13C-bicarbonate in tumour-bearing rat brain in vivo. Therefore it could have major clinical significance in assessing the efficacy of such therapies. However, it should be recognised that DCA may have very limited clinical applications as an anti-cancer drug due to its toxicity. – QA

Clinical Colorectal Cancer

Treatment of pulmonary colorectal metastases by radiofrequency ablation

Petre E, Jia X, Thornton R et al. Clinical Colorectal cancer 2013;12(1):37-44.

The lung is the second commonest site for colorectal metastases, with 10% of patients developing lung secondaries during the course of their disease. Metastasectomy is generally regarded as the gold standard treatment with reported 5 year survival of 41-56% in selected patients. However many patients are unsuitable for resection due to age, infirmity or lung co-morbidity; recovery may be prolonged and beset by complications. Furthermore, many patients develop further lung lesions and repeat resection is challenging. Previous reports suggest that radiofrequency ablation (RFA) can achieve good local control but numbers are small and follow-up short. This study from Memorial Sloane Kettering Cancer Center in New York looks at 45 patients with a median age of 63 (range 43-81) years who underwent RFA for 69 lung metastases <3.5cm in diameter between 2004 and 2010;. Most had previous or concurrent liver metastases; 36 patients had already undergone chemotherapy and 24 had had surgery for their lung lesions. None were eligible for resection. RFA was delivered to 1-3 lesions in one lung under general anaesthesia on an ambulant basis: where necessary artificial pneumothorax was induced to separate the lesion from mediastinum or chest wall. The commonest complication of RFA was pneumothorax (in a third of patients); there was no mortality associated with treatment. Disease control was monitored by PET/CT at one month and 3-monthly thereafter: median follow-up was 18 months.Nine lesions progressed on follow-up: 4 were successfully retreated, with 92% of patients showing no progression at one year. The median overall survival was 46 months from RFA and 132 months from resection of the colorectal primary. Actuarial survival was 95%, 72% and 50% at 1, 2 and 3 years respectively. The best outcomes were seen in patients with few metastases and those <1.5cm in diameter.

Reviewer's opinion: The limitations of this study are self-evident – it is a retrospective analysis of a relatively small group of patients, treated using a variety of different algorithms. Survival following RFA appears inferior to the best results from metastasectomy, but these figures are achievable only in highly selected patient cohorts and should not be compared to the more familiar patients with multiple metastatic sites and significant comorbidity upon whom this study was based. The authors conclude that RFA can achieve good local control of pulmonary metastases, and propose a randomised comparison with Stereotactic radiotherapy. – JRN

Diary of Events

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

September

Lymphoedema: Core Skills and Knowledge (Level 3)
3 September 2013; Glasgow, UK
Margaret Sneddon
T: +44 (0)141 330 2072
E: lymph@glasgow.ac.uk

Bone Research Society/British Orthopaedic Research Society Joint Meeting
4-5 September 2013; Oxford, UK
E: events@brsoc.org.uk
W: www.brsoc.org.uk

Clinical Radiology Annual Scientific Meeting 2013
9-11 September 2013; London, UK
W: www.rcr.ac.uk

RCR Clinical Oncology Annual Meeting
10 September 2013; London, UK
E: conf@rcr.ac.uk
T: +44(0)20 7299 130
F: +44(0)20 7323 3100
W: www.rcr.ac.uk/onc-annual-meeting

NEW
6th Annual Royal Marsden Breast Cancer Meeting: Hot Topics in Breast Cancer
13 September 2013; London, UK
W: www.royalmarsden.nhs.uk/breastmeeting

NEW
Radiotherapy Study Day
16 September 2013; London, UK
W: www.royalmarsden.nhs.uk/radiotherapy

Personalised Medicine & Cancer Treatment
16 September 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

2nd Annual Conference on Cancer Vaccines
18-19 September 2013; London, UK
W: Smi-online.co.uk

NEW
20th International Congress of Hepatic Surgeons from ex-USSR countries
28-20 September 2013;
Donetsk, Ukraine
E: stepanovaua@mail.ru
W: www.hepatoassociation.ru or www.congress2013.dn.ua

Edinburgh MRCS Preparation Course
21-22 September 2013;
Edinburgh, UK
W: www.christie.nhs.uk/school-of-oncology/education-events
T: +44 (0)161 446 3773 or
E: education.events@christie.nhs.uk

ASTRO's 55th Annual Meeting
22-25 September 2013;
Georgia, Atlanta, USA
W: www.astro.org

NEW
Developing Communication Strategies to Support Self-Management in Cancer Patients
23 September 2013; London, UK
W: www.royalmarsden.nhs.uk
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921.

Cancer & Cardiology for GP's
23 September 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

5th ORBS International meeting
23-25 September 2013;
Nottingham, UK
E: admin@orbsmeetings.com

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

Ovarian cancer and the Leah Lederman lecture and Annual General Meeting
25 September 2013; London, UK
W: www.rsm.ac.uk

NEW
RSM: Progress towards individualised cancer treatments
26 – 27 September 2013;
London, UK
W: rsm.ac.uk

Teenage & Young Adults in Oncology
26 September 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
Progress towards individualised cancer treatments
26-27 September 2013; London, UK
W: rcr.ac.uk

NEW
Radiotherapy – Meeting the current workforce challenges for patient care
27 September 2013; London, UK
W: rcr.ac.uk

NEW
Masterclass: Sexual difficulties associated with breast cancer and its treatment
27 September 2013; London, UK
W: www.breastcancercare.org.uk

Joint 17th ECCO – 38th ESMO – 32nd ESTRO European Cancer Congress
27 September – 1 October, 2013;
Amsterdam, The Netherlands
W: www.ecco-org.eu

NEW
International Cancer Imaging Society Meeting & 13th Annual teaching Course
30 September-2 October 2013;
London, UK
W: rcr.ac.uk

October

NEW
Anaesthesia for Major Surgery Conference
1 October 2013; London, UK
W: www.royalmarsden.nhs.uk/anaesthesia

Future Innovations in Treatment for Colorectal Cancer
2 October 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
Interpretation of the Plain Chest X-Ray
5 October 2013; London, UK
W: www.royalmarsden.nhs.uk/chestxray
E: conferencecentre@rmh.nhs.uk
T: +44 (0)020 7808 2921

The Christie FRCR Part 2B Preparation Course
5-6 October 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

18th ESGO International Meeting
5-8 October 2013; Athens, Greece
W: www.esgo.org

BLS Conference 2013
6-8 October 2013; Birmingham, UK
W. www.thebls.com
T: +44 (0)1452 790178

NEW
Innovations in Cancer Research
9 October 2013; London, UK
W: www.royalmarsden.nhs.uk/innovations
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

NEW
Focus on Symptoms in the Child with Advanced Cancer
15 October 2013; London, UK
W: www.royalmarsden.nhs.uk/childsymptoms
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

NEW
The Royal Marsden Palliative Care Update
16 October 2013; London, UK
W: www.royalmarsden.nhs.uk/palliativeupdate
E: conferencecentre@rmh.nhs.uk
T: +44 (0)20 7808 2921

Living with Sexuality & Cancer
16 October 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
Head and Neck Cancer: From Diagnosis To Palliative Care
16 October 2013;
St Catherine's Hospice
E: education@stcatherines.co.uk

NEW
Kidney and Prostate Cancer Conference
17 October 2013; London, UK
W: www.royalmarsden.nhs.uk/kidneyprostate

Introduction to lymphoma for nurses
17 October 2013; Maidstone, UK
E: healthprofessionals@lymphomas.org.uk or
W: www.lymphomas.org.uk/health-professionals/conferences

NEW
Teleconference: An update on bone metastases
18 October 2013
W: www.breastcancercare.org.uk

16th Annual BOPA Symposium
18-20 October 2013; Edinburgh, UK
W: www.bopawebsite.org

NEW
Understanding Our Connective Tissue System (Level 2)
19-21 October 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
7th UK Radiation Oncology Conference (UKRO)
21–23 October 2013;
Nottingham, UK
W: www.ukro.org.uk

Haematology Nurse Study Day (Acute Myeloid Leukaemia)
21 October 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

Management of Central Venous Access Devices
24 October 2013; Middlesex, UK
E: anni.hall@nhs.net

NEW
International Society of Geriatric Oncology (SIOG)
24-26 October 2013;
Copenhagen, Denmark
W: www.siog.org

THNO

4th Trends in Head and Neck Oncology

7-9 November 2013

Valamar Lacroma, Dubrovnik, Croatia

www.headandneckoncology2013.org

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ANNOUNCEMENT

BTOG 2014

12th Annual BTOG Conference 2014

Wednesday 29th to Friday 31st January 2014
The Burlington Hotel, Dublin

Important Dates

Registration Opens Online
1st September 2013

Poster Abstract Submission Opens Online
1st September 2013

Poster Abstract Submission Closes Online
31st October 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 Bone Disease in Lung Cancer Study Day

Thursday 17th October 2013
Hotel Russell, London

Registration is free
– Travel Bursaries are available
– visit www.btog.org for details

This study day will cover the diagnosis, care and treatment of lung cancer patients with bone disease. CPD points will be applied for. Amgen has provided sponsorship and a travel bursary to enable this meeting to take place. Amgen has had no input into the agenda, selection of topics or speakers or in to the disbursement of the travel bursary.

British Thoracic Oncology Group (BTOG) is a lung cancer and mesothelioma research group. The principal aim of BTOG is to encourage the development of clinical and scientific research in all areas of Thoracic Oncology and the provision of a multi-disciplinary educational forum. All individuals involved in any aspect of lung cancer or mesothelioma research, treatment or care are eligible to become members of the Group.

BTOG Secretariat

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BTOG 2014 Information is available on the website:

www.BTOG.org

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