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IN THIS ISSUE

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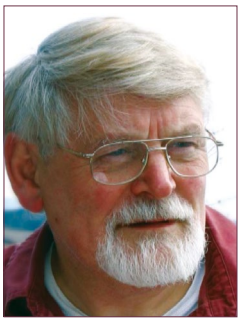

Denys Wheatley
Editor.

Oncology News – Moving Forward into 2018 The 'oncologynews' team

The previous editorial brought you up to date with the position the journal was in as it went through transition. The good news is that an excellent management team has been brought together, about which there will be more as we get the January/February issue together (volume 13 (1), 2018). It has been a tough task to get everything transferred to the team over the last six weeks, which is why the last issue (November/December, 2017 – volume 12 (4) will only be appearing in mid-January. One of our most difficult problems has been getting the emails of all readers and subscribers updated, which now numbers about 7,000. As we go global, this number should increase significantly during 2018.

For our online publication, https://www.oncologynews.biz, we will continue to include advertisements, event notices and reports, information on cancer charities, comments on topical news, diaries, reviews of pertinent research papers and books; all of these will be in addition to our core of regular articles on all aspects of cancer and cancer-related topics. For example, cancer-care professionals will value the magazine's practical and accessible approach, a popular way to keep up-to-date with the latest developments in such aspects as care of the skin in some cancerous conditions, or special massage techniques. Our portal for submissions is editor@oncologynews.biz.

Apart from articles, a small handling fee will have to be charged for most of these items other than commercial advertising, for which a rate card is available on request. We can also assist your immediate needs with a fast track mailshot to our subscribers. For more information, contact our Marketing and Advertising Manager at info@oncologynews.biz.

Oncology News has an excellent following, with contributions from many different experts and authorities. Its assistant editor is Dr Richard Ablin, discoverer of prostate specific antigen, unfortunately and misleading misnamed in Roswell Park Cancer Institute as prostate cancer specific antigen. It is only a corollary factor in the possibility that malignant changes might be occurring in the prostate gland. Our neuro-oncology section is looked after by Professor Geoff Pilkington. We will have many more expert panels in the coming years from all part of the world on the vast range different malignancies that continue to plague mankind, i.e. watch this space!

Denys Wheatley

Professor Denys Wheatley, BSc (Lond), PhD, DSc, MD (multi h.c.), CIBiol, FRSB, FCPath, is Chairman and Director of BioMedES UK, and is now in charge of the management team publishing *Oncology News* under the auspices of his company. BioMedES (pronounced like Archimedes) also publishes another online journal, *Cancer Hypotheses*, the content of which is theoretical papers on all aspect of cancer from carcinogenesis to the putative mechanism of the action of anti-cancer drugs and other interventions. It acts as a forum for debate, with articles having critical comments on old or extant theories, and particularly welcomes papers positing new hypotheses.

Denys has a long history of editing scientific and medical journals ever since his postgraduate days in the Institute of Cancer Research (The Chester Beatty) in London. He ran *Cell Biology* International for over 16 years, and founded two online journals in the early days of online publishing through BioMed Central (*Cancer Cell International* and *Theoretical Biology and Medical Modelling*). In 1998 he formed Cancer Treatments International with Dr Slobodan Tepic (Davös and Zürich), before it became Bio-Cancer Treatments International in Hong Kong, for which he was Chief Scientific Officer for its first 10 years. The development from it of pegylated L-arginase in the treatment of hepatocellular carcinoma, melanoma and AML is now undergoing further trials in the USA and UK, as well as Hong Kong. He also perceptively noted the role of the primary cilium as a major player in cell sensory activity, and the fact that its dysfunction would result in pathological conditions. It is now implicated in ~50 disorders, from polycystic kidney disease to dementia, although this cellular organelle had for the best part of a century been considered rudimentary or vestigial.

His research has taken him all over the world, often in recent times to Hungary, Brazil, Russia, Ukraine and USA. He continues to collaborate with colleagues worldwide in the development of new cancer treatments. In publishing and scientific communication, he has taught courses in about 20 different countries on *Scientific Writing and Publishing* (his Manual of this title is available on Amazon Kindle). As well as receiving international awards for his research and many offices in international and national organisations, he has received three doctorates (honoris causa), published over 350 papers and 6 books, with two more in preparation.

As an artist, he has given many exhibitions, especially in helping people needing art in therapy or mental health recovery. He plays (cello) regularly with the Aberdeen Chamber Orchestra and the European Doctors Orchestra, and performed in the inaugural and second concert of the World Doctors Orchestra in Berlin and Cleveland, respectively.

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Leggat House,
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Publisher & Editor:
Dr Denys Wheatley
editor@oncologynews.biz
T: +44 (0)1467 670280
www.oncologynews.biz

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On the cover: Jenny Agutter – patron of "Ovacome" (Photograph by courtesy of Ming Yeung)

Ovacome – a charity focusing on women with ovarian cancer – "get tealed!"

'Have you been tealed?' is the ovarian cancer charity "Ovacome" (www.ovacome.org.uk) publicity and social media campaign this March; it ties up with Ovarian Cancer Awareness Month. Professional cameraman and editor of Getty Images Ming Yeung, whose wife Rebecca has ovarian cancer, has shot celebrities included herein, the actors Jenny Agutter – Ovacome's patron (cover) – and Nigel Havers, with socks in teal – the colour chosen to represent the disease.

The idea is that women should ask themselves if they have been tealed, shorthand for knowing the symptoms of the disease, which the charity outlines in the easier to remember acronym BEAT: **B** is for bloating that is persistent, it does not come and go; **E** is for difficulty in eating, and feeling full too quickly; **A** is for abdominal and pelvic pain felt most days; and **T** is for toilet changes in urination or bowel habits.

In its study of 324 women, Ovacome found that, despite bloating being the most common symptom of ovarian cancer followed by abdominal pain, women are more likely to seek medical help when they have abdominal pain (47%) or a change in urination (25%). Ovacome's chief executive, Victoria Clare, said "We know that women recognise the symptoms of bloating, but often dismiss it as being something less sinister. It is understandable that they often only seek advice because it is less easy to ignore pain, but this mind-set needs to change."

Contact: www.ovacome.org.uk

Photo credit: Ming Yeung

Nigel Havers, appropriately wearing teal-coloured socks, a good match!

Shaun Mansfield
Biovault Technical Ltd and University College London, Department of Biochemical Engineering.

Correspondence address:
E: smansfield@biovault.com

Role of Hematopoietic Stem Cells in the Treatment of Hemato-Oncological Disease

Hematopoietic stem cells (HSCs) are multipotent adult stem cells that can differentiate into myeloid and lymphoid lineages, for example erythrocytes, platelets and T-cells (Figure 1) in a process known as Hematopoiesis. They reside within the bone marrow (BM) throughout life and are responsible for continued Hematopoiesis. There they make up part of the stem cell niches within the bone marrow along with mesenchymal stromal cells (MSCs). The purpose of the stem cell niche is to regulate proliferation, differentiation and maturation of the cells, providing lifelong blood cell production.

When the BM and/or the HSCs are damaged, a condition known as aplastic anaemia, a deficiency in erythrocytes, leukocytes and thrombocytes is seen. Severe aplastic anemia can be fatal left untreated; one course of treatment is to replace the damaged BM and HSCs using HSC transplant (HSCT).

Since the first successful BM transplant in 1956 was carried out by Dr Edward Donnall Thomas, HSCTs have become an established, sometimes curative, treatment for over 80 malignant and non-malignant conditions, including acute myeloid leukaemia [1] and non-Hodgkin's lymphoma [2].

Three sources of HSCs exist – BM, PB and umbilical cord blood (UCB) – all sources that have been used clinically for both autologous and allogenic HSCTs. Each source has its own distinct advantages and disadvantages; for example, a BM collection is more invasive to the donor than a PB collection, which is more invasive than an UCB collection.

Hematopoietic Stem Cell Transplant (HSCT)

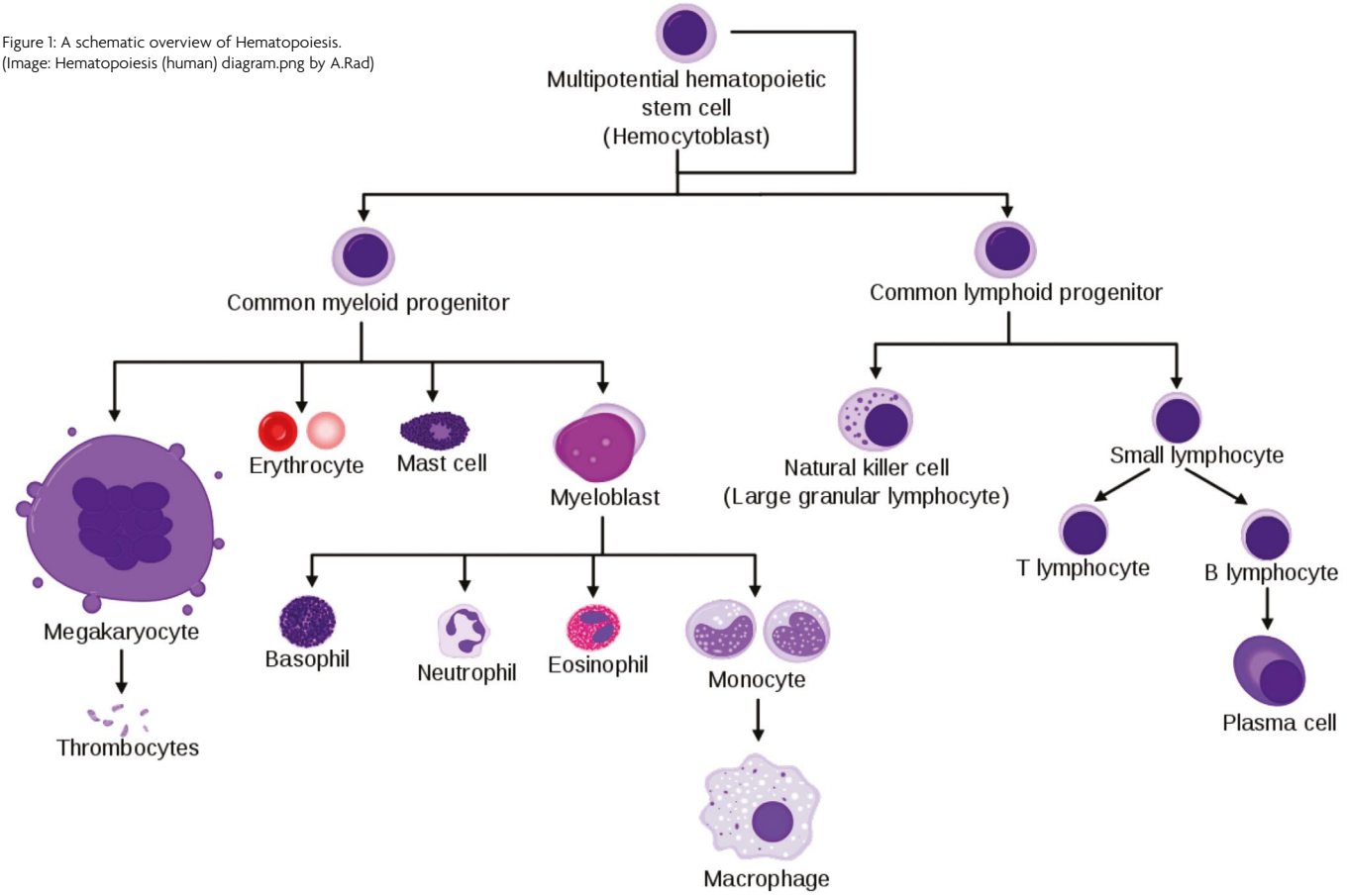
HSCTs are routinely used worldwide, with over 40,000 HSCTs taking place annually in Europe alone.

Currently PB HSCTs are the most commonly used transplants. The procedure can involve both autologous and allogenic transplants, as well as the administration of granulocyte colony-stimulating factor (G-CSF). G-CSF results in the mobilisation of HSCs into the peripheral blood, from where they can be collected, although the mechanism by which this mobilisation occurs

Table 1: List of the advantages of UCB transplants over peripheral blood and bone marrow transplants

Advantage	**Description**
Ease of Collection	When compared to BM and PB, which are both invasive collection procedures, the method for collection of UCB is simpler and non-invasive. UCB is typically considered to be clinical waste and as such, is disposed of.
Lower Risk of Disease Transmission	UCB transplants have a reduced likelihood of transmission of common viral pathogens such as cytomegalovirus and Epstein-Barr virus.
HLA Mismatching is well Tolerated	In contrast to BM and PB transplants where an 8/8 match is required, HLA mismatches on one or two loci are well tolerated in UCB transplants. This increases the number of potential recipients for one UCB unit.
A Large Repository of Donors can be Established	UCB is collected at the time of birth, transported to a processing facility and cryopreserved with all routine testing completed e.g. viral screening. When required the UCB unit can be assigned to the patient without the lengthy wait of locating a suitable voluntary donor.
Decreased Risk of GvHD	The immune cells within UCB are less likely to initiate an immune response against the patient's own tissue.

Figure 1: A schematic overview of Hematopoiesis.
(Image: Hematopoiesis (human) diagram.png by A.Rad)



is not fully understood. However, it is thought that an increase in activated proteolytic enzymes results in the loss of anchorage of HSCs from the stem cell niche. Once mobilised, the HSCs can be isolated from the peripheral blood using an apheresis process, in which the peripheral blood is removed from the donor and passed through an apheresis machine that separates the PB retaining the mononuclear cells (MNCs) that contain the HSCs, and then returning the remaining blood products to the patient. The resulting PB-HSC product is either transplanted directly into the patient in the case of allogenic HSCTs, or cryopreserved and administered after preparative treatment in the case of autologous HSCTs.

A HSCT can be performed after myeloablative or non-myeloablative preconditioning. Myeloablative preconditioning involves the use of total body irradiation (TBI) and/or high dose chemotherapy. In these treatments, the tumour cells are removed; however, it results in severe immune deficiency in the patients. The role of the HSCT in myeloablative preconditioning is to engraft in the BM and reconstitute the patient's immune system. For the elderly and those medically unfit to withstand TBI and/or high dose chemotherapy, non-myeloablative and reduced intensity preconditioning regimes have been developed. In these cases, the HSCT initiates a graft versus tumour (GvT) affect, whereby the transplant initiates an immune response against the tumour cells.

Umbilical Cord Blood (UCB)

In lieu of a suitable HLA-matched donor for a BM or PB HSCT, UCB provides an alternative source of HSCs; in fact since the first successful UCB transplant in 1988 for the treatment of aplastic anemia, over 35,000 units have been transplanted worldwide [3].

UCB-HSCs have distinct advantages over the other sources, including a decrease in the risk or severity of graft-versus-host disease (GvHD) and the ability to generate a large repository of units for transplantation. The method of collection compared to BM or PB, as described above, is significantly easier and uses what is normally considered clinical waste and consequently is discarded. The advantages of UCB are summarised in Table 1.

Despite these advantages the major drawback of UCB is the number of HSCs contained within one unit, typically 5-10% of the dose obtained from BM and PB. This disadvantage leads to an increased time to neutrophil and platelet engraftment, ~30 and 50-100 days, respectively [4]. This increases the hospitalisation time and therefore the treatment cost, as well as increasing the risk of graft failure, opportunistic infections and transplant related mortality (TRM).

UCB is a one-time transplant and additional UCB from the same donor cannot be obtained. This removes the ability to perform a donor lymphocyte infusion (DLI) if required. A DLI is a procedure where lymphocytes from the original HSCT donor are transplanted to support the GvT effect. The DLI reduces the growth and mount an anti-tumour immune response against any residual tumour cells.

Overcoming the Limitations of UCB

To overcome the limitations of UCB as a source of HSCs, the administration of two UCB units has become common clinical practice in adults, where the dose of HSCs required is higher. This effectively doubles the dose of HSCs available; however, as two units are required to be administered, this increases the treatment cost and is reliant on a readily available supply of UCB units. However, this seems to improve transplant outcomes and as such there is a long-term cost benefit that may outweigh the initial treatment cost.

An alternative method to increasing the cell dose is ex vivo expansion. The ex vivo expanded UCB can then be administered as a standalone graft or with an unmanipulated unit. Ex vivo expansion uses cell culture supplemented with growth factors, cytokines and small molecules. The combination of supplements that provide optimal results has yet to be elucidated.The list includes stem cell factor (SCF), thrombopoietin (TPO) and FMS-like tyrosine kinase 3 ligand (FLT-3-L) as a base and additional supplements: it also includes IL-3, IL-6, Stem Regenin-1 (SR1) and G-CSF.

Work thus far has demonstrated than an expanded UCB product, when administered with an unmanipulated unit , can improve early hematopoietic recover; however, the unmanipulated unit is responsible for the long-term engraftment. The ability to administer a single ex vivo expanded product that improves early hematopoietic recovery and is responsible for long-term recovery is desirable as it eliminates any potential adverse reactions with the administration of cells from different donors. Clinical trials are still in progress.

Conclusion

Over the last 60 year HSCTs have played a vital role in modern medicine and have provided treatment for a considerable number of patients, improving their quality of life and extending life expectancy. Whilst the limitations of UCB remain a impasse, significant work on improving outcomes has been completed, which has resulted in the outcomes in adult patients with hematologic malignancies receiving an UCB HSCT comparable to that of a matched unrelated PB or BM HSCT [5]. With this fact and the continued effort for improvement, a question arises - is it ethical to subject a donor to the invasive collection procedures required for PB and BM harvests when UCB is a viable option?

REFERENCES

1. Cornelissen, J. J. & Blaise, D. *Hematopoietic stem cell transplantation for patients with AML in first complete remission.* Blood 127, 62–70 (2016).
2. Carella, A. et al. *Autografting Followed by Nonmyeloablative Immunosuppressive Chemotherapy and Allogeneic Non-Hodgkin's Lymphoma.* Lancet, The 18, 3918–3924 (2000).
3. Ballen, K. K., Verter, F. & Kurtzberg, J. *Umbilical cord blood donation: public or private?* Bone Marrow Transplant. 50, 1271–1278 (2015).
4. Danby, R. & Rocha, V. *Improving engraftment and immune reconstitution in umbilical cord blood transplantation.* Front. Immunol. 5, 1–19 (2014).
5. Horwitz, M. E. & Frassoni, F. *Improving the outcome of umbilical cord blood transplantation through ex vivo expansion or graft manipulation.* Cytotherapy 17, 730–738 (2015).

Specialist massage for cancer patients

Jennifer Young,
BSc, Hons in Biology
Jennifer Young & Beauty Despite Cancer.
Jennifer received post-graduate qualifications in Occupational Health and Law. She is a qualified massage therapist, beauty therapist, product formulator and nutritional therapist. Jennifer developed the new massage for cancer patients qualifications as a reaction to being unable to find evidence to support the prohibition of specialist touch therapies for cancer patients. She has been recognised by the Courts as an expert in Occupational Health and control of cross infection.

Correspondence address:
E: jennifer@jenniferyoung.co.uk

Massage for cancer patients is a controversial subject. Massage therapists are taught that cancer is a contraindication to massage. The same is true of facials, manicures and all other holistic and beauty therapies. Therapists are taught not to touch cancer patients, yet they are usually able to access complementary therapies in clinical settings. Therapists are also unable to get insurance to do so. The benefits of these treatments are well documented: Summary of the benefits of massage to those going through treatment for cancer.

Short-term benefits, as reported from different sources:

- Reduced anxiety, depressed moods and anger in breast cancer patients [1,2,4,9].
- Increased vigor [2] (breast cancer patients).
- Reduced mood disturbances and perceived stress levels [3].
- Improved sleep quality [4,9].
- Improved quality of life [4] (breast cancer patients).
- Reduced pain and improvement of mood, reduced stress levels [5,9].
- Reduced perception of pain, nausea and increased relaxation after 10 minute (5 minute per foot) foot massage [6].
- Pain intensity, pulse rate, and respiratory rate significantly reduced immediately after massage. At study entry, the massage group reported higher pain intensity, which decreased by 42% (25% reduction in the control group) [7].
- Reduced anxiety scores, depression, general fatigue, reduced motivation fatigue, and emotional fatigue [8].
- Reduced depression and improved sleep [10].
- Reduced heart rate [11] and lower blood pressure [11].
- Decrease in physical discomfort, group fatigue, and mood disturbance. The effect of massage on mood disturbances was greater when treated continuously by the same therapist [12].

Long-term benefits:

- Reduced depression and hostility, increased urinary dopamine, serotonin levels, natural killer cell number and lymphocytes in breast cancer patients [1,2].
- Reduced mood disturbances and perceived stress levels [3] (breast cancer patients).

There appears to be no evidence to suggest that adapted massage carried out by specialist massage therapists is potentially harmful to those going through treatment for cancer. Macmillan have published the following advice, as have Cancer Research UK:

'Some people worry that massage could cause cancer cells to spread to other parts of their body. Research has not found any evidence of this....' [13]

'Some people worry that having a massage when you have cancer may make the cancer cells travel to other parts of the body. No research has proved this to be true'. [14]

Cancer Research UK suggest the following as possible side-effects of massage for those going through treatment for cancer:

'Most people don't have any side effects from having a massage. You may feel a bit light headed, sleepy, tired or thirsty afterwards. Your massage therapist may advise you to drink a glass of water when your treatment has finished and you feel thirsty. They usually allow you to get ready to leave in your own time so that you don't have to rush. Some people find that they feel a bit emotional or tearful for a while afterwards'. [14]

Both charities emphasise the need for cancer patients to visit specially trained massage therapists who can adapt the massage to meet their needs [13,14].

Specialist training has been developed to allow the provision of complementary therapies in spas, salons, clinics and therapy rooms. This has many benefits including allowing patients to access therapies outside of the clinical setting. Patients often report a desire to enjoy the same services that they used prior to diagnosis. Until the recent advent of specialist and accredited qualification, this has been impossible.

The new qualifications address the following concerns:

- Hygiene and control of cross infection
- Appropriate pressure
- Contraindications – local and general
- Areas to avoid
- How to converse with a cancer patient
- Making a client comfortable
- Identification and control of hazards to the therapist
- Record keeping

It gives some useful background to:

- Cancer
- Cancer treatment
- Common side-effects of treatment

- Medical devices.
- Specialist skincare products for cancer patients.
- Natural ingredients that should not be included in skincare products used on those living with a cancer.

The fully referenced training aims to lets the therapist welcome all affected by cancer to their services, safely and with professional assurance.

REFERENCES

1. Hernandez-Reif, M., Ironson, G., Field, T., Katz, G., Diego, M., Weiss, S., Fletcher, M., Schanberg, S. & Kuhn, C. (2003). *Breast cancer patients have improved immune functions following massage therapy.* Journal of Psychosomatic Research, 57, 45-52.
2. Hernandez-Reif, M., Field, T., Ironson, G., Beutler, J., Vera, Y., Hurley, J., Fletcher, M., Schanberg, S., Kuhn, C., & Fraser, M. (2005). *Natural killer cells and lymphocytes increase in women with breast cancer following massage therapy.* International Journal of Neuroscience, 115, 495-510
3. Listing, M., Krohn, M., Liezmann, C., Kim, I, Reisshauer, A., Peters, E., Lapp, B.F. & Rauchfuss, M. (2010). *The efficacy of classical massage on stress perception and cortisol following primary treatment of breast cancer.* Arch Womens Ment Health. Apr;13(2):165-73.
4. Sturgeon, M., Wetta-Hall, R., Hart, T., Good, M., & Dakhil, S. (2009). *Effects of therapeutic massage on the quality of life among patients with breast cancer during treatment.* Journal of Complementary Medicine, 15, 373-380.
5. Hodgson, N.A., & Lafferty, D. (2012). *Reflexology versus Swedish Massage to Reduce Physiologic Stress and Pain and Improve Mood in Nursing Home Residents with Cancer: A Pilot Trial.* Evidence-Based Complementary and Alternative Medicine, 2012, 5 pages
6. Grealish, L., Lomasney, A., & Whiteman, B. (2000). *Foot massage. A nursing intervention to modify the distressing symptoms of pain and nausea in patients hospitalized with cancer.* Cancer Nursing, 23, 237-243.
7. Wilkie, D.J., Kampbell, J., Cutshall, S., Halabisky, H., Harmon, H., Johnson, L.P., Weinacht, L., & Rake-Marona, M. (2000). *Effects of massage on pain intensity, analgesics and quality of life in patients with cancer pain: A pilot study of a randomized clinical trial conducted within hospice care delivery.* Hospice Journal, 15, 31-53.
8. Rexilius, S.J., Mundt, C., Erickson Megel, M., & Agrawal, S. (2002). *Therapeutic effects of massage therapy and handling touch on caregivers of patients undergoing autologous hematopoietic stem cell transplant.* Oncology Nursing Forum, 29, 35-44.
9. Smith, M.C., Kemp, J., Hemphill, L., & Vojir, C.P. (2002). *Outcomes of therapeutic massage for hospitalized cancer patients.* Journal of Nursing Scholarship, 34, 257-262.
10. Soden, K., Vincent, K., Craske, S., Lucas, C., & Ashley, S. (2004). *A randomized controlled trial of aromatherapy massage in a hospice setting.* Palliate Medicine, 18, 87-92.
11. Billhult, A., Lindholm, C., Gunnarsson, R., Stener-Victorin, E. (2009). *The effect of massage on immune function and stress in women with breast cancer--a randomized controlled trial.* Autonomic Neuroscience, 150, 111-115.
12. *Massage therapy reduces physical discomfort and improves mood disturbances in women with breast cancer.* Psycononcology, 18, 1290-1299.
13. http://www.macmillan.org.uk/information-and-support/coping/complementary-therapies/complementary-therapies-explained/massage-therapies.html accessed 12th April 2015
14. http://www.cancerresearchuk.org/about-cancer/cancers-in-general/treatment/complementary-alternative/therapies/massage-therapy accessed 12 April, 2014.

Established in 1963, the Society has grown into the national charity for cancer care, and is the leading provider of information relating to cancer prevention, detection, treatment and support. We also advocate for improvements in cancer. The charity is governed by a voluntary Board of Directors of medical experts, scientists and business people, is responsible for overall control and strategic direction of the charity, and is advised by several expert committees.

Each year in Ireland there are around 40,000 new cancer cases and by 2020, one in two of us will be diagnosed with a cancer in our lifetime. As numbers increase, so does the need for services that provide information and support for patients and their families. The Irish Cancer Society provides a range of cancer support services. Our Cancer Nurseline Freephone 1800 200 700 is open Monday-Friday 10am-4pm, giving confidential advice, support and information on a range of topics through booklets and online resources. Our Daffodil Centres are located in 13 hospitals nationwide, staffed by cancer nurses and trained volunteers.

Our Survivor Support Programme offers peer support from those diagnosed with cancer. Our trained volunteers are available to provide emotional and practical support to anyone going during and after treatment. We also work with cancer support groups nationwide to ensure cancer patients have access to confidential support, including counselling. We provide practical and financial support for patients in need and undergoing treatment through our Travel2Care, Financial Support and Volunteer Driver Programmes. Four in ten cancer cases are preventable, and cancer risk can be reduced by adopting certain lifestyles. Educating people and supporting them should help to reduce the number of new cancer cases each year. Our National public awareness campaigns focus on early detection, signs and symptoms, and lifestyle influences on cancer risk. We also provide a range of community-based programs to increase awareness of how risk can be reduced; for example, X-HALE is our smoking prevention program for young people, We Can Quit supports women helping others to stop smoking, and Fit For Work and Life is our 12-week community health and well-being program for people seeking employment.

One in four deaths in Ireland each year is from cancer. With such an incidence, people need proper support in place to help them to a dignified death. Our Night Nursing service provides end-of-life care for cancer patients in their own home, surrounded by family and loved ones. It is the only service of its kind in the Ireland. Because of the generous support of the public, the Irish Cancer Society is the largest voluntary funder of cancer research in Ireland. Since 2010, over €20 million has been invested in research projects. Collaboration, both national and international, is at the core of Irish Cancer Society Research.

For more information visit www.cancer.ie; you call our Cancer Nurseline on 1800 200 700.

Daiichi Sankyo – Phase 1 Data for EZH1/2 Dual Inhibitor DS-3201 in Patients with Non-Hodgkin Lymphomas

Preliminary exploratory efficacy results from phase 1 study show an overall response rate of 58.8% with single agent DS-3201, an investigational and potential first-in-class EZH1/2 dual inhibitor, in patients with relapsed or refractory non-Hodgkin lymphomas.

An overall response rate of 45.5% (five of 11 patients) was observed with DS-3201 in 11 evaluable patients with B-cell lymphomas, including follicular lymphoma (five patients), diffuse large B-cell lymphoma (three patients), extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (two patients) and lymphoplasmacytic lymphoma (one patient). An overall response rate (ORR) of 83.3% (five of six patients) was observed with DS-3201 in six evaluable patients with T-cell lymphomas, including peripheral T-cell lymphoma not otherwise specified (two patients), angioimmunoblastic T-cell lymphoma (two patients) and adult T-cell leukemia-lymphoma (two patients).

A separate study of DS-3201 is also underway in the US in patients with AML and ALL, underscoring Daiichi Sankyo Cancer Enterprise's commitment to advancing science for blood cancers.

Preliminary exploratory efficacy results from an ongoing phase 1 dose escalation study showed that an ORR of 58.8% (10 of 17 patients) was observed with single agent DS-3201 in 17 evaluable patients with NHLs, including B-cell and T-cell lymphomas, who were relapsed from or refractory to standard treatment or for whom no standard treatment was available. Among the ten patients with response, there were one complete remission and nine partial remissions. Additionally, four patients experienced stable disease and three patients experienced progressive disease.

"Based on these preliminary safety and efficacy data on DS-3201 in a clinical setting, further evaluation of DS-3201 is warranted. As the first dual inhibitor of EZH1 and EZH2 in clinical development, DS-3201 may represent a new epigenetic approach to treating blood cancers. We look forward to reviewing additional data as it becomes available to evaluate the potential of this approach." said Dai Maruyama, MD, PhD, Department of Hematology, National Cancer Center Hospital, Tokyo, Japan.

Following observation of dose-limiting toxicities (DLTs) in three of 18 evaluable patients, dose expansion is ongoing to determine a conclusive recommended phase 2 dose. Four DLTs were observed in three patients who received either the 200 or 300mg dose: there were three cases of temporary grade 4 platelet count decreases (one patient in the 200mg cohort and two patients in the 300mg cohort) and one case of grade 3 anemia requiring transfusion in a patient in the 300mg cohort. Preliminary safety data from 18 evaluable patients in the study also were reported. The most common treatment emergent hematologic adverse events of any grade seen in all patients included decreased platelet count (77.8%), anemia (55.6%), decreased lymphocyte count (50.0 percent) and decreased neutrophil count (44.4%). The most common treatment emergent non-hematologic adverse events were dysgeusia (50.0%), alopecia (33.3%), diarrhea (22.2%), decreased appetite (22.2%), nasopharyngitis (22.2%), alanine aminotransferase increased (22.2%), rash (16.7%), aspartate aminotransferase increased (16.7%) and dry skin (16.7%). One serious adverse event of grade 3 pneumocystis jirovecii pneumonia (PJP) led to discontinuation from the study. There was one additional non-serious case of PJP observed, leading to the institution of prophylactic treatment for all subsequent patients enrolled into the study.

DS-3201 targets epigenetic regulation by inhibiting both the EZH1 (enhancer of zeste homolog 1) and EZH2 (enhancer of zeste homolog 2) enzymes, which may reactivate various genes that have been silenced by the protein H3K27me3.1 Reactivation of the silenced genes has been shown to result in decreased proliferation of EZH2-expressing cancer cells. Preclinical research has shown that DS-3201 suppressed trimethylation of H3K27 in cells (IC50: 0.55 nM) more potently than EZH2 selective inhibitors [1].

"Targeting epigenetic regulation is an approach to treating cancer that aims to reverse aberrant epigenetic changes that contribute to cancer cell growth and to maintain normal gene expression. The dual inhibition of EZH1/2 is theoretically able to provide a different spectrum of activity compared to EZH2-specific inhibitors already in the clinic. Our phase 1 program is designed to address the question of the potential benefit for this dual mode of action. In addition to the phase 1 study in non-Hodgkin lymphomas, we also are evaluating targeting epigenetic regulation with DS-3201 in patients with acute myeloid leukemia and acute lymphocytic leukemia" said Antoine Yver, MD, MSc, Executive Vice President and Global Head, Oncology Research and Development, Daiichi Sankyo.

Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma (NHL) is a form of cancer that originates in lymphocytes, a type of white blood cell [2]. The two main types of NHL are B-cell lymphomas and T-cell lymphomas, which are classified into subtypes based on the origin and stage of the cancer [2]. There were an estimated 386,000 new cases and about 200,000 deaths globally from NHL in 2012 [3]. In Japan, there were nearly 21,000 new cases of NHL in 2012, accounting for around five percent of cases worldwide [3]. While recent treatment advances have led to improved outcomes for patients with certain types of NHL, patients with aggressive NHL subtypes or relapsed or refractory disease still face a poor prognosis [2,4].

About the DS-3201 Phase 1 Study

A multicenter, non-randomised, open-label phase 1 dose escalation trial in Japan is enrolling adult patients with non-Hodgkin lymphomas (NHL) who have relapsed from or are refractory to standard treatment or for whom no standard treatment is available. The primary objectives are to evaluate the safety and pharmacokinetics of multiple-dose monotherapy of DS-3201 and to determine the recommended phase 2 dose. Secondary objectives are to determine the maximum tolerated dose of DS-3201 and to conduct exploratory evaluations of DS-3201-related biomarkers and the efficacy of DS-3201. ***For more information about the clinical trial, visit ClinicalTrials.gov.***

About DS-3201

Part of the AML Franchise of the Daiichi Sankyo Cancer Enterprise, DS-3201 is an investigational and potential first-in-class EZH1/2 dual inhibitor in phase 1 clinical development for hematologic cancers including acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL) and

non-Hodgkin lymphoma (NHL). DS-3201 is an investigational agent that has not been approved by the FDA or any other regulatory agency worldwide as a treatment for any indication. Safety and efficacy have not been established.

About Daiichi Sankyo Cancer Enterprise

The vision of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking in order to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by our Antibody Drug Conjugate (ADC) and Acute Myeloid Leukemia (AML) Franchises, our cancer pipeline includes more than 20 small molecules, monoclonal antibodies and ADCs stemming from our powerful research engines: our two laboratories for biologic/immuno-oncology and small molecules in Japan, and Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley, CA. ***For more information, please visit: www.DSCancerEnterprise.com.***

About Daiichi Sankyo

Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address diversified, unmet medical needs of patients in both mature and emerging markets. With over 100 years of scientific expertise and a presence in more than 20 countries, Daiichi Sankyo and its 15,000 employees around the world draw upon a rich legacy of innovation and a robust pipeline of promising new medicines to help people. In addition to a strong portfolio of medicines for hypertension and thrombotic disorders, under the Group's 2025 Vision to become a "Global Pharma Innovator with Competitive Advantage in Oncology," Daiichi Sankyo research and development is primarily focused on bringing forth novel therapies in oncology, including immuno-oncology, with additional focus on new horizon areas, such as pain management, neurodegenerative diseases, heart and kidney diseases, and other rare diseases. For more information, please visit: www.daiichisankyo.com. Daiichi Sankyo, Inc., headquartered in Basking Ridge, New Jersey, is a member of the Daiichi Sankyo Group. ***For more information on Daiichi Sankyo, Inc., please visit: www.dsi.com.***

References

1. Honma D, et al. *ASH Annual Meeting.* Abstract #2073. 2017.
2. American Cancer Society. *Non-Hodgkin's Lymphoma.* 2017.
3. Ferlay J, et al. *GLOBOCAN 2012 v1.0.* Cancer Incidence and Mortality Worldwide; IARC CancerBase No. 11. 2013.
4. Chao M. Cancer Manag Res. 2013;5:251-269.

Contact: Jennifer Brennan, Daiichi Sankyo, Inc.
E: jbrennan2@dsi.com T: +1 908 992 6631.

Scancell Holdings Plc and Cancer Research UK collaborate to advance novel cancer immunotherapy into clinical trials

Cancer Research UK is about to take SCIB2 into a Phase 1/2 trials for patients with a range of solid tumours

Scancell Holdings PLC, a developer of novel immunotherapies for the treatment of cancer, and Cancer Research UK, the world's leading cancer charity, are pleased to announce that they have entered into a Clinical Development Partnership to develop Scancell's ImmunoBody® vaccine, SCIB2, for the treatment of patients with solid tumours, including non-small cell lung cancer (NSCLC).

Scancell's ImmunoBody® immunotherapy platform activates the body's immune system by enhancing the uptake and presentation of cancer antigens to help target and eliminate cancer cells. SCIB2, Scancell's second ImmunoBody® therapy, targets an antigen called NY-ESO-1, which is expressed on a range of solid tumours, including NSCLC and oesophageal, ovarian, bladder and prostate cancers, as well as neuroblastoma, melanoma and sarcoma.

Under the terms of the Clinical Development Partnership, Cancer Research UK will fund and sponsor a UK-based Phase 1/2 clinical trial of SCIB2 in combination with a checkpoint inhibitor in patients with solid tumours, focusing on NSCLC in the first instance. The charity's Centre for Drug Development (CDD) will be responsible for manufacturing the clinical trial supplies of SCIB2, conducting pre-clinical testing, sponsoring and managing the clinical trial, including the clinical trial timelines.

Following completion of the Phase 1/2 clinical trial, Scancell will have the option to acquire the rights to the data to support further development of SCIB2 itself. If Scancell elects not to exercise the option, Cancer Research UK will retain the right to take the SCIB2 programme forward in all indications.

Professor Lindy Durrant, Chief Scientific Officer of Scancell, commented: "We are delighted to announce this partnership with Cancer Research UK, which is a significant endorsement for our ImmunoBody® technology. The charity's world-renowned expertise will no doubt be invaluable as we progress SCIB2 through the clinic. In pre-clinical studies, we have shown that a combination of SCIB2 and checkpoint inhibition produces enhanced tumour destruction and significantly longer survival times than when either treatment was used alone. We believe SCIB2 has the potential to provide a much needed treatment option for patients suffering from a range of common solid tumours."

Dr Nigel Blackburn, Cancer Research UK's director of drug development, said: "We're excited to be giving our extensive expertise and experience in drug development to move this immunotherapy treatment into the clinic.

"This collaboration will ensure that this innovative vaccine reaches patients sooner and could bring about urgently needed improvements for some cancers which can be hard to treat, including lung cancer – a disease where survival rates remain stubbornly low."

About Scancell

Scancell is developing novel immunotherapies for the treatment of cancer based on its ImmunoBody® and Moditope® technology platforms. Scancell's first ImmunoBody®, SCIB1 is being developed for the treatment

of melanoma. Data from the Phase 1/2 clinical trial demonstrate that SCIB1, when used as monotherapy, has a marked effect on tumour load, produces a melanoma-specific immune response and highly encouraging survival trend without serious side effects. In patients with resected disease there is increasing evidence to suggest that SCIB1 may delay or prevent disease recurrence.

Scancell's ImmunoBody® vaccines target dendritic cells and stimulate both parts of the cellular immune system: the helper cell system where inflammation is stimulated at the tumour site, and the cytotoxic T-lymphocyte or CTL response where immune system cells are primed to recognise and kill specific cells.

Pre-clinical data on a combination of SCIB1 or SCIB2 and checkpoint inhibition (blockade of the PD-1 or CTLA-4 immune checkpoint pathways) have shown enhanced tumour destruction and significantly longer survival times than when either treatment was used alone.

Scancell has also identified and patented a series of modified epitopes that stimulate the production of killer CD4+ T cells that have the ability to destroy tumours with minimal toxicity. The Directors believe that the Moditope® platform could play a major role in the development of safe and effective cancer immunotherapies in the future.

About Cancer Research UK's Clinical Development Partnerships

CDP is a Cancer Research UK initiative that aims to develop promising anti-cancer agents from companies that are not able to take them through early phase clinical trials themselves. Under the scheme, Cancer Research UK sponsors and funds early clinical development, while companies retain all underlying rights to their programmes. At the end of the study, companies can decide if they wish to develop the drug further based on the clinical trial results. If they choose not to, the charity may secure an alternative partner and ensure the drug has every possible chance of reaching patients, with a share of future income returned to Cancer Research UK.

Cancer Research UK's Centre for Drug Development

Cancer Research UK has an impressive record of developing novel treatments for cancer. The Cancer Research UK Centre for Drug Development, formerly the Drug Development Office, has been pioneering the development of new cancer treatments for 25 years, taking over 140 potential new anti-cancer agents into clinical trials in patients. It currently has a portfolio of around 30 new anti-cancer agents in preclinical development, Phase I or early Phase II clinical trials. Six of these new agents have made it to market including temozolomide for brain cancer, abiraterone for prostate cancer and rucaparib for ovarian cancer. Two other drugs are in late development Phase III trials. This rate of success is comparable to that of any pharmaceutical company.

About Cancer Research UK

Cancer Research UK is the world's leading cancer charity dedicated to saving lives through research. Cancer Research UK's pioneering work into the prevention, diagnosis and treatment of cancer has helped save millions of lives. Cancer Research UK receives no government funding for its life-saving research. Every step it makes towards beating cancer relies on vital donations from the public. Cancer Research UK has been at the heart of the progress that has already seen survival in the UK double in the last 40 years. Today, two in four people survive their cancer for at least 10 years. Cancer Research UK's ambition is to accelerate progress so that by 2034, three in four people will survive their cancer for at least 10 years. Cancer Research UK supports research into all aspects of cancer through the work of over 4,000 scientists, doctors and nurses. Together with its partners and supporters, Cancer Research UK's vision is to bring forward the day when all cancers are cured.

For further information about Cancer Research UK's work or to find out how to support the charity, please call 0300 123 1022 or visit www.cancerresearchuk.org. Follow us on Twitter and Facebook.

Sam Purewal
Sam.Purewal@fticonsulting.com Intern, Life Sciences, FTI Consulting
www.fticonsulting.com
200 Aldersgate, Aldersgate Street London EC1A 4HD. T: +44 (0)20 331 95700.

For Further Information:
Dr John Chiplin, Executive Chairman
Dr Richard Goodfellow, CEO
Scancell Holdings Plc
T: +1 858 900 2646
T: +44 (0)20 3727 1000
Freddy Crossley (Corporate Finance)
Tom Salvesen (Corporate Broking)
Panmure Gordon (UK) Limited
T: +44 (0)20 7886 2500

Mo Noonan/Simon Conway
FTI Consulting
T: +44 (0)20 3727 1000
Kathryn Ingham (Press Office)
Cancer Research UK
T: +44 (0)20 3469 5475

Xenikos BV report on phase I/II trial with T-Guard™ for treatment of steroid-resistant acute GVHD

Xenikos BV disclosed detailed efficacy and safety data from a clinical phase I/II trial with T-Guard for the second-line treatment of steroid-resistant acute graft-versus-host disease (GVHD).

- Fifty percent day 28 complete responses (CR) and 60% overall survival (OS) at six months in high-risk patient population with 90% lower gastrointestinal tract involvement.
- Rapid recovery of the immune system with a diverse T cell repertoire.

A Phase I/II Study on the Anti-CD3/CD7 Immunotoxin Combination (T-Guard™) for the Treatment of Steroid-Refractory Acute GVHD has been presented by Walter JFM van der Velden, Radboud University Medical Center. Nijmegen, The Netherlands, Seventeen of the 20 patients (85%) in this study suffered from severe steroid resistant-acute GVHD (Grade III-IV), and all had involvement of their visceral organs – gut (18/20; 90%) and liver (5/20; 25%). Twelve of these patients (60%) achieved an overall clinical response (ORR) on day 28, with 10 patients (50%) achieving a complete response (CR). Twelve of the 20 patients were alive at s months (overall survival, (OS), at this time, 60%). The outcomes compared favorably with the most recent historical controls of the participating centers, receiving either infliximab (N=21) or inolimomab/etanercept (N=21), where an ORR and CR was achieved in 52 and 19% of patients, respectively, and OS at six months was 29%. The one-week treatment course resulted in marked in vivo T- and NK-cell depletion, followed by a rapid recovery of the immune system starting right after the last T-Guard infusion with increasing T- and NK-cell numbers and a diverse T cell repertoire, suggesting a rebalancing of the immune system.

Dr van der Velden said that "With a long-term survival rate of only 20%, there is an urgent need for more effective therapies for steroid-refractory acute graft-versus-host disease, especially for those that limit the level of immune suppression after achieving a remission. Indeed, today there are no approved therapies to treat acute GVHD once a patient becomes resistant to or the disease progresses following treatment with steroids. T-Guard has demonstrated promising response rates and overall survival results, allowed for a swift immune reconstitution and proved to be safe and well tolerated. I look forward to the initiation of the pivotal trial with T-Guard, which, if proven safe and effective, I believe could be a potentially game-changing therapy.

We are excited about the data from this important clinical study, providing further evidence for the potential of T-Guard to effectively treat stem cell transplantation patients with this life-threatening medical complication," said Ypke van Oosterhout, PhD, Chief Executive Officer of Xenikos. "We look forward to discussing the results from the phase I/II trial with FDA soon and gaining their input on the design of the pivotal international phase III trial, which we plan to initiate in the first half of 2018 and that is expected to support a future regulatory filing for marketing approval in both the US and Europe."

The study enrolled 20 adult patients with a median age of 53, all of whom had received an allogeneic stem cell transplant for myeloid or lymphoid malignancies, and had Grade II-IV steroid-resistant acute GVHD. Patients were treated with T-Guard administered as a four-hour intravenous infusion every 48 hours for a total of four infusions (4mg/m^2 each). The primary efficacy endpoint was defined as ORR on day 28. Main secondary endpoints were CR rate at day 28 and six-month OS, as well as safety and tolerability.

Treatment with a short course of T-Guard was generally well tolerated with no significant infusion reactions. There was a limited number of potentially T-Guard-related adverse events, which consisted of thrombocytopenia, micro-angiopathy and hypoalbuminemia. The adverse events were manageable and reversible after treatment.

The Company is planning to initiate a pivotal multi-center global active-controlled trial, comparing T-Guard with best-available therapy for steroid-resistant acute GVHD in the first half of 2018.

About Acute Graft-versus-host Disease

Patients who have had an allogeneic stem cell transplant are at high risk of developing graft-versus-host disease (GVHD). The older the person is, the higher the risk for GVHD. GVHD develops when the donor's immune cells mistakenly attack the patient's normal cells. Acute GVHD can occur soon after the transplanted cells begin to appear in the recipient and ranges from mild or moderate to severe, and can be life-threatening if its effects are not controlled. While patients may be successfully treated with steroids, once the disease progresses or if a disease is resistant to treatment, there are currently no approved therapies. The long-term survival of patients with steroid-resistant acute GVHD is only 20% (Calmettes et al., BBMT, 2015); thus, there is an urgent need to develop more effective therapies for this disease.

About T-Guard™

T-Guard is in development for the treatment of steroid-resistant acute graft-versus-host disease (GVHD), a life-threatening immune condition. T-Guard consists of a combination of two toxin-loaded antibodies that target CD3 and CD7 on T and NK cells and shows promise as a therapeutic tool for safely and swiftly rebalancing the body's immune system in T-cell-mediated diseases. Once injected into the body, T-Guard specifically identifies and eliminates adult T- and NK-cells, with a strong preference for the activated T cells. In preclinical testing, T-Guard was shown to be highly effective in killing these cells through non-inflammatory apoptotic mechanisms (programmed cell death), which are associated with minimal side effects. T-Guard's brief but targeted action is believed to leave patients less vulnerable to opportunistic infections when compared to current best available but not yet approved therapies. T-Guard has been granted Orphan Drug Designation in both the EU and US.

Xenikos recently completed a phase I/II study in 20 patients with severe steroid-refractory acute GVHD. Based on

the results, the Company believes that T-Guard has the potential to offer a curative approach with a one-week treatment. Unlike other approaches, which only address symptoms, T-Guard actively restores the immunological balance, providing a durable remedy for patients with this devastating and potentially fatal disease. A registration trial for this indication is expected to start in the first half of 2018. Other areas of future development may include transplant-related rejection, acute solid organ rejection and various severe autoimmune diseases.

About Xenikos B.V.

Xenikos B.V. is developing new, innovative immunotherapies to help restore patients' health and save lives. It is developing new therapies based on the action of conjugated antibodies that enables patients suffering from serious immune diseases or rejection after transplantation to reset their immune systems quickly and efficiently. Its lead product candidate T-Guard is currently being developed for the second-line treatment of steroid-resistant acute GVHD. ***Further information is available at www.xenikos.com.***

For further information:
Corporate contact:
Xenikos B.V.
Ypke van Oosterhout, PhD,
Chief Executive Officer.
T: +31 24 3000100
E: y.vanoosterhout@xenikos.com

MC Services AG:
Dr. Solveigh Mähler,
T: +49 211 529 252 19
E: solveigh.maehler@mc-services.eu

For US inquiries:
Laurie Doyle:
T: +1 339 832 0752
E: laurie.doyle@mc-services.eu

Genetic link found between the immune system and lymphoma

DNA changes identified include several previously associated with autoimmune disease.

From The Institute of Cancer Research, London

In a recent study by scientists at The Institute of Cancer Research, London, they found that people who inherit genetic changes that alter the function of their immune system have a higher risk of developing Hodgkin lymphoma than the rest of the population, being one of the most common cancers in young adults. Six genetic changes are involved, but many of DNA changes can affect the function of the immune system, and three of the genes implicated had previously been associated with autoimmune diseases (e.g. multiple sclerosis, rheumatoid arthritis, lupus). The six changes noted were single base changes in DNA linked to the development of Hodgkin lymphoma, five of which affect the development of B-cells, the cells that are involved in producing antibodies. Clear differences in genetic risk were noted between two different subtypes of Hodgkin Lymphoma, namely nodular sclerosis Hodgkin Lymphoma (NSHL) and mixed cellularity Hodgkin Lymphoma (MCHL). For example, a single base change located in DNA near the gene LPP increased the risk of NSHL by 37%, but had little effect on the risk of developing MCHL.

The researchers stressed that the link did not mean people with autoimmune diseases are at increased risk of lymphoma, but did offer important genetic clues for understanding both lymphoma and autoimmune diseases better. Professor Richard Houlston, head of the Molecular and Population Genetics, said that "Interestingly, we found that some of the genetic changes we have linked to Hodgkin lymphoma have previously been associated with the risk of autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis.

One of the genetic changes identified increases the risk of Hodgkin lymphoma by more than a third, and the others each by at least 15%, information that could point to new targeted drugs for the disease. The findings were published in Nature Communications. The research was funded by a several organisations, including Bloodwise, Cancer Research UK, and the Lymphoma Research Trust. The analysis was made on genetic data from 5,314 cases of Hodgkin lymphoma and 16,749 controls, collating data from four different European investigations, one of the largest ever carried out. For most people, Hodgkin lymphoma can be successfully treated with first-line therapies, but new treatments are needed for cases where first-line treatment has failed.

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, remarked that "Understanding the genetic changes that underpin cancer's development is crucial for all aspects of our quest to defeat cancer – to understand which patients are most at risk from different types of cancer, to improve diagnosis, and to develop treatments that are most likely to work for individual patients."

Dr Alasdair Rankin, Director of Research at Bloodwise, said that "Because of research, treatments for many people with Hodgkin lymphoma are now good, and around 80% of all people affected survive in the long-term. Although this is good news, treatments can have long-term health effects, such as infertility and secondary cancers, so finding kinder treatments for Hodgkin lymphoma is important. We welcome this study, which sheds new light on how Hodgkin lymphoma develops."

The Royal Marsden NHS Foundation Trust in its 'bench-to-bedside' approach has intimate association with the ICR making it possible to get results in a way that other institutions cannot. Together these two organisations are rated in the top four centres for cancer research and treatment in the world.

For more information please contact Claire Hastings in the ICR press office on 020 7153 5380 or claire.hastings@icr.ac.uk. For enquiries out of hours, please call 07595 963 613.

University College London Hospital on Truxima® (CT-P10, biosimilar rituximab) in patients with advanced-stage follicular lymphoma

CT-P10 also proven to have pharmacokinetic equivalence to reference rituximab.

New data from University College London Hospitals NHS Foundation Trust (UCLH) on the safety and tolerability of rapid infusion of CT-P10 show that rapid infusion of CT-P10 is well-tolerated across all patient groups, and patients could be safely switched from reference rituximab to CT-P10 without reverting to slower infusion rates [1].

An independent study examined the infusion-related reactions (IRRs) in three different patient groups: rituximab naive, those switching directly from reference rituximab to CT-P10, and those that received their last dose of reference rituximab at least six months prior to the study [1]. Administration of rituximab is associated with IRRs which occur most frequently during the first infusion. To reduce the risk of IRRs, it is the manufacturers' recommendation that the first dose is increased every 30 minutes in 50mg/hour increments resulting in a typical rituximab infusion taking four to six hours. It is common practice however to administer rituximab as a rapid infusion if the first infusion is well-tolerated which reduces infusion time to just over an hour and 30 minutes [1].

Simon Cheesman from the University College London Hospitals NHS Foundation Trust and one of the authors of the study said, "We felt that it was important to investigate the safety of using rapid infusion for CT-P10 as this method of infusion for reference rituximab is of significant benefit to patients, taking hours off their treatment time. The findings from the study should help to increase physician confidence and facilitate the introduction of CT-P10 at centres prescribing rituximab across the UK and beyond".

Man Hoon Kim, President and CEO of Celltrion Healthcare, welcomed the findings from UCLH's study commenting: "The study by UCLH is of significant importance as it demonstrates that CT-P10 can be safely administered as a rapid infusion without physicians having to revert to the slower infusion rate. This not only saves hospitals' valuable time and resources but also greatly improves the patient experience".

Celltrion Healthcare presented pharmacokinetic (PK) data for CT-P10, which compared the PK properties of CT-P10 and reference rituximab according to several relevant clinical factors in patients with advanced-stage follicular lymphoma. The results showed that the PK of CT-P10 is in accordance with historical data about reference rituximab and further supports the PK similarity between CT-P10 and reference rituximab across all patient sub-groups [2].

About CT-P10 (biosimilar rituximab)

CT-P10 is a mAb that targets CD20, a transmembrane protein found on the surface of most B cells. By binding specifically to CD20, CT-P10 depletes B cells by three main mechanisms: Induction of apoptosis, stimulation of CDC (complement-dependent cytotoxicity) and stimulation of ADCC (antibody-dependent cell-mediated cytotoxicity).

CT-P10 is approved in the EU for the treatment of patients with non-Hodgkin lymphoma (NHL), chronic lymphocytic leukaemia, rheumatoid arthritis, granulomatosis with polyangiitis and microscopic polyangiitis. Further details of the approved indications and safety information for CT-P10 are available in the summary of product characteristics (SmPC) [3].

About Advanced FL

Follicular lymphomas are the second most frequent subtype of nodal lymphoid malignancies in Western Europe [4] and are a subtype of NHL [5]. It is a slow-growing lymphoma that develops from B lymphocytes (B cells). It is characterised by painless swelling of the lymph nodes, fever for no apparent reason, drenching night sweats, fatigue, infections and bleeding. Most cases are advanced at the time of diagnosis but since the advent of rituximab, overall survival has increased to in excess of 20 years. It is called 'follicular' lymphoma because the abnormal lymphocytes often collect in lymph nodes in clumps that are known as 'follicles'. Follicular lymphoma is more common in people aged over 65, but it can occur in people of any age.

About CT-P10 Advanced FL 24 week study [6]

This Phase III, randomised, parallel-group, active-controlled, double-blind study aims to demonstrate equivalence of pharmacokinetics and non-inferiority of efficacy for CT-P10 in comparison with reference rituximab, each administered in combination with cyclophosphamide, vincristine, and prednisone (CVP) in patients with advanced FL.

A total of 121 patients were included in the results presented at the ASH meeting [2]. Fifty-nine patients in the CT-P10 group and 62 patients in the reference rituximab group received CT-P10 or reference rituximab plus CVP every three weeks over eight cycles. No statistically significant differences were found between the two groups in PK properties in all subgroup analyses.

Data previously published in The Lancet, Hematology, in 2017 showed that CT-P10 was non-inferior to reference rituximab in advanced FL in terms of efficacy [7].

About Celltrion Healthcare

Celltrion Healthcare conducts the worldwide marketing, sales and distribution of biological medicines developed by Celltrion, Inc. through an extensive global network that spans more than 120 different countries. Celltrion Healthcare's products are manufactured at state-of-the-art mammalian cell culture facilities, designed and built to comply with the US Food and Drug Administration (FDA) cGMP guidelines and the EU GMP guidelines.

For more information please visit: http://www.celltrionhealthcare.com

References

1. Shah et al. *Evaluation of the Safety and Tolerability of Rapid Infusion of Biosimilar Rituximab Truxima® - the University College London Hospitals (UCLH) Experience.* 59th Annual Meeting of the American Society of Hematology (ASH). 2017. 3387.
2. Won Seog Kim et al. *Clinical Factors Impact on Pharmacokinetics of CT-P10 and Reference Rituximab in Patients with Advanced-Stage Follicular Lymphoma.* 59th Annual Meeting of the American Society of Hematology (ASH). 2017. 1504.
3. *Truxima concentrate for solution for infusion summary of product characteristics* [last accessed December 2017]. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/004112/WC500222694.pdf.
4. Dreyling, M, et al. *Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.* Ann Oncol. 2016;27(suppl 5):v83-v90 doi:10.1093/annonc/mdw400.
5. Kohrt HEK & Ugarte A. *Follicular Lymphoma: a Guide for Patients. European Society for Medical Oncology.* 2014. Available at: https://www.esmo.org/content/download/52236/963497/file/EN-Follicular-Lymphoma-Guide-for-Patients.pdf [accessed December 2017].
6. *Phase 3, Randomised, Parallel-Group, Active-Controlled, Double-Blind Study to Demonstrate Equivalence of Pharmacokinetics and Noninferiority of Efficacy for CT-P10 in Comparison With Rituxan, Each Administered in Combination With Cyclophosphamide, Vincristine, and Prednisone (CVP) in Patients With Advanced Follicular Lymphoma* [last accessed December 2017]. Available at: https://clinicaltrials.gov/ct2/show/NCT02162771.
7. Won Seog Kim et al. *Efficacy, pharmacokinetics, and safety of the biosimilar CT-P10 compared with rituximab in patients with previously untreated advanced-stage follicular lymphoma: a randomised, double-blind, parallel-group, non-inferiority phase 3 trial.* The Lancet Haematology 4.8 (2017): e362-e373.

SOTIO, a Biotechnology Company Owned by the PPF Group Broadening of its Phase II Clinical Trial Program in Ovarian Cancer

In Prague, November 28, 2017, Sotio announced the enrolment of the first patient to a Phase II study testing DCVAC/OvCa in combination with standard of care chemotherapy for patients with ovarian cancer after first relapse. Based on positive signals from ongoing trials, SOTIO is also expanding its ongoing study testing DCVAC/OvCa as a maintenance therapy in first-line treatment of patients with ovarian cancer. This newly initiated clinical trial SOV06 (Eudra CT: 2017-002196-26) is an open-label, single-group, multicenter Phase II clinical trial evaluating DCVAC/OvCa in combination with standard of care chemotherapy in women with first relapse of platinum-sensitive epithelial ovarian carcinoma.

The SOV06 study will enrol 30 patients in seven oncogynecological centres. The clinical trial is conducted in collaboration with CEEGOG (Central and Eastern European Gynecological Oncology Group), which brings together centres dedicated to patients with malignant gynecological tumours in 8 Central and Eastern Europe countries. The first patient was enrolled in the clinical trial at the General University Hospital in Prague in the department of Professor David Cibula: "For CEEGOG this is an exceptional study for several reasons. The active substance was developed in the Czech Republic, where the sponsor, biotechnology company SOTIO, is headquartered; the mechanism of action is innovative and the results of studies conducted so far are promising in the area, which still has the worst results in our field of gynecological oncology,"

SOTIO is expanding its ongoing trial SOV01 (Eudra CT: 2013-001322-26) by including additional 30 patients in the Czech Republic. SOV01 is a randomised, open-label, three-arm multicentre Phase II clinical trial evaluating DCVAC/OvCa in combination with first-line standard chemotherapy in women with newly diagnosed epithelial ovarian cancer after radical debulking surgery. The trial was launched in November 2013, recruitment being completed in March 2016. The first part of SOV01 enrolled 99 patients at clinical sites in the Czech Republic, Poland and Germany.

Ladislav Bartonicek, CEO of SOTIO, said: "Positive signals from the clinical trials with DCVAC/OvCa encourage us to launch an additional Phase II trial with more patients to confirm its efficacy. The expansion of the clinical trials represents an important step in the development of this innovative treatment for ovarian cancer. We have also started discussions with key opinion leaders to define the path towards the setup of the registration trials." Radek Spisek, Chief Scientific Officer of SOTIO added: "SOV06 and the expansion of SOV01 represent a significant broadening of our Phase II program for ovarian cancer. From ongoing clinical trials we see indications that DCVAC/OvCa in combination with the first-line chemotherapy could be beneficial for patients. Expanding the program and testing of DCVAC/OvCa in combination with standard of care chemotherapy in patients with platinum sensitive relapse of the disease is a logical step to do."

About DCVAC

DCVAC is an active cellular immunotherapy treatment produced for each patient using the patient's own dendritic cells to induce an immune reaction against tumour antigens. SOTIO is developing three product candidates using the DCVAC platform to affect multiple different cancers in various stages of disease – DCVAC/PCa for patients with prostate cancer, DCVAC/OvCa for patients with ovarian cancer and DCVAC/LuCa for patients with lung cancer. The company is currently testing the safety and efficacy of investigational medicinal treatment DCVAC through multiple Phase I to Phase III clinical trials. SOTIO has been sponsoring 4 Phase II clinical trials in patients with ovarian cancer (DCVAC/OvCa treatment).

About SOTIO

SOTIO is an international biotechnology company leading the efforts of PPF Group to build a diverse biotechnology portfolio through its own research & development, collaborations, in-licensing, investments, mergers and acquisitions. The company is developing new medical therapies, focusing on the treatment of cancer and autoimmune diseases. SOTIO's most advanced project is its proprietary platform of active cellular immunotherapy (ACI) based on dendritic cells. SOTIO is also collaborating with NBE Therapeutics on the development of novel antibody-drug conjugate products (ADC), with Cytune Pharma on developing novel IL15-based immunotherapies for the treatment of cancer, and with LDC and Max Planck on an oncology program addressing a novel target in tumour metabolism. SOTIO has facilities in Europe, the United States, China and Russia.

Contact: Richard Kapsa, Head of Communication,
T: (+420) 224 174 448. E: kapsa@sotio.com

UKCRC Tissue Directory and Coordination Centre of BioBanking

The UK Clinical Research Collaboration (UKCRC) Tissue Directory and Coordination Centre (the Centre) aims to coordinate Biobanking activities in the UK. The Centre represents a first step in integrating national biobanking infrastructure to support research activity. ***You can read more about the project and how to get involved at https://www.biobankinguk.org***

A joint vision

Biomedical researchers rely on human tissue samples for a multitude of research projects; cancer is of particular note as it such a heterogeneous disease. Given the development of precision medicine and the need for more reliable disease models in other fields, the demand for high quality samples and associated data will increase over time. Until now, there has been no coordinated effort to catalogue or coordinate human biosample acquisition and storage. The Centre was established in 2014 by the UK Clinical Research Collaboration (UKCRC) Experimental Medicine Funders Group in order to achieve their Vision for Human Tissue Resources.

The funder's vision

"Funders aim to maximise the value of human tissue samples and resources while minimising duplication of effort. This requires better characterisation of tissue samples, asking for generic consent, and increased linkage to accurate clinical data. Sample collections must then be made more easily discoverable and accessible for use in high quality, ethical research."

The Centre has therefore been established to promote best practice, harmonisation and standardisation, and increase sample visibility in the hope that this will lead to increased sharing of samples, creating a more efficient research environment in the UK.

The UKCRC Tissue Directory

Launched in 2016, the UK-wide Tissue Directory, is a first step in promoting access to samples for research. The directory contains the details of biological samples and data held across >80 biobanks in the UK. The directory aims to facilitate communication between researchers and biobanks, providing a quick and efficient route for researchers to access appropriate samples and data to match their research needs.

Researchers can search the online directory and locate appropriate tissue samples held by a specific biobank, based on the associated datasets giving age and gender of donors, and sample type. It is possible to search the directory using the specific disease term by viewing the list of diseases or the A-Z of Biobanks.

The Centre does not facilitate sample access; it acts as a platform for promoting visibility of existing resources.

An ethical duty to share

The UK Ethics Committee Authority (UKECA) has now made registration in the UKCRC Tissue Directory a condition of the Research Ethics Committee (REC) favourable opinion for research tissue banks (RTB). Patients gift their samples, under the impression that they will be used for scientific medical research. This change in the terms of REC favourable opinion should lead to a shift in the culture of research. Dr Philip Quinlan has said: "It is fantastic that the UKCRC Tissue Directory and Coordination Centre has been recognised as the best centre to do this work; tissue banks will have an ethical obligation to ensure their sample collections are visible to the community and we hope this will lead to better coordination between biobanks ensuring more samples are contributing directly to medical progress." Indeed, this is the first ever defined expectation for researchers to register the existence of the samples they hold.

Award winning engagement

The Centre actively engages with all stakeholders through events, campaigns and communications to ensure the development of the project provides plenty of information. The centre works with people and organisations to promote best practice, governance and public engagement.

The Centre has run a number of successful road-shows at institutions around the country to promote its work and encourage feedback. The Centre's most recent annual meeting was held on the 16th November at the Oval in London. UK Biobanking Showcase was a unique opportunity to bring together all stakeholders in the field and featured debates, give talks and award the prestigious "Biobank of the Year".

2016 saw the centre in parliament at a Biobanking event: "The Biobanking time-bomb; maintaining public trust in medical research". The aim of this event was to address the future risks to biobanking if certain issues were not addressed. These risks include the reducing contributions from Research grants to Biobanks, cost recovery being insufficient to recover financial deficits, particularly due to the increasing cost of running biobanks. Reward mechanisms and access to clinical data are also important issues that were discussed. Find out more about the event on our website.

As well as engaging with Biobanks and policy makers, The Centre has an active public engagement programme. Project and Engagement manager, Jessica Sims, has developed a Board game to explain biobanking to the public. This innovative approach to a complex and sensitive issue has won public engagement awards in the past. Ms Sims says "public understanding is vital to tissue donation. I wanted to develop a way of really engaging with people in a format they can understand". Contact Ms Sims at j.sims@ucl.ac.uk to learn more about the game,

BBMRI.uk

The Biobanking and BioMolecular Resources Research Infrastructure (BBMRI) – European Research Infrastructure Consortium (ERIC; BBMRI-ERIC) – is one of the largest research infrastructures for health in Europe today. It provides services and expertise for its members, including expert centres, events, and a European sample locator. They have also coordinated a number of research projects within Europe and beyond.

The Centre represents the UK and engages with this network on ethical, legal and societal issues (ELSI), IT and Quality common service groups. It has also contributed to the drafting of sample quality standards along with BBMRI-ERIC. Visit their website or get in touch to find out more about getting involved with this network.

To get involved

The Centre in the UK relies on the research community to shape our work; it is therefore keen to engage with pathologists, particularly those involved in biobanking on

how you can help (contact in email below). You can register your samples online at https://directory.biobankinguk.org. There are more resources including the latest biobanking news and advice at https://www.biobankinguk.org. Finally, you can also sign up to The Centre's Newsletter for all the latest news and events.

Dr Emma Lawrence
Engagement Manager, Research
The UKCRC Tissue Directory and Coordination Centre
9/316, Royal Free Hospital,
Pond St, London NW3 2QG
E: contact@biobankinguk.org

**Staff: Dr Phil Quinlan, Director, The UKCRC Tissue Directory and Coordination Centre.*
Ms Jessica Sims, Engagement Manager, Collaborations, The UKCRC Tissue Directory and Coordination Centre.

Breaking bad: cancer cell drug addiction solved

From The Netherlands Cancer Institute

Cancer cells can become not only resistant to, but addicted to the drugs that try to kill them. A research team led by Professor Daniel Peeper from the Netherlands Cancer Institute has now discovered the underlying mechanism, which may guide the development of more rational alternating therapies.

Because cancers can become resistant to therapy, this presents a major challenge to patient care. Sometimes, however, cancers are not only resistant to, but can become addicted to the very drugs used to treat them. Indeed, research on patients, animal models and cultured cells have suggested that this dependency is a double-edged sword in that it can work against tumours; drug-addicted cells can die massively when treatment is suddenly stopped. Although this is a potential new approach, the mechanism of addiction was unknown, at least until now.

Breaking addiction

To understand the mechanism of cancer drug addiction, it is probably best to try to break it, argued group leader Daniel Peeper and his postdoc Xiangjun Kong at the Netherlands Cancer Institute. They used melanoma cells that were both resistant and addicted to a treatment based on the inhibition of BRAF, a common driver of malignancy. With a technique called CRISPR-Cas9, they knocked out all individual genes in the cancer cell genome one by one. They searched for cells carrying a mutation that had broken the addiction, which were those that had managed to survive when treatment was discontinued, whereas all others died. With this strategy, the researchers identified a signaling pathway vital for drug addiction, involving the proteins ERK2, JUNB, and FRA1. Peeper said "Interestingly, all resistant tumour cells we examined used this same drug addiction mechanism, irrespective of how they had become resistant. When this pathway is disrupted, cancer cells overcome their drug addiction. We have demonstrated this in both cell culture and tumour-bearing mice, and we have indications of the same phenomenon is seen in patients with drug-resistant melanoma. This mechanism was active in lung cancer cells that were addicted to another drug. This suggests that the pathway we uncovered may be important for various cancer types and treatments."

Rational alternating treatments

Unfortunately, cancer cells are very flexible and can often reverse their addiction themselves. The new findings may be used to target those addicted cancer cells that fail to die upon stopping the treatment. "Instead of giving addicted cells a break, we should probably immediately switch to another treatment", says Peeper. "Now that we understand how cancer cells can overcome their drug addiction, we have a solid basis for identifying the most effective second treatment for this so-called alternating therapy approach."

His team have started with melanoma cells addicted to a BRAF-inhibitor. They stopped this treatment and subsequently treated the cells with the chemotherapeutic agent, dacarbazine. This combination of sudden drug withdrawal and a second treatment turned out to be more effective than just discontinuing the first treatment. Peeper remarked that "This was a proof-of-principle experiment in cultured cells demonstrating how effective these alternating treatments may be. It sets the stage for systematic studies identifying which treatments cooperate best with drug withdrawal for therapy-addicted cancers."

The work was financially supported by the Dutch Cancer Society and the European Research Council. ***For more information or interview requests, please contact Sanne Hijlkema, Science Information Officer at the Netherlands Cancer Institute (communicatie@nki.nl, +31 20 512 28 50).***

About The Netherlands Cancer Institute

The Netherlands Cancer Institute has been at the international forefront of cancer care and research for more than a century. The unique combination of healthcare and scientific research within the same institute offers great benefit for cancer patients. Specialised cancer care professionals work together in multidisciplinary teams to set up and carry out treatment plans tailored to the needs of individual patients because no two tumours are alike. Cancer patients or people suspected of having cancer can come to our hospital, known as the Antoni van Leeuwenhoek, to make use of this personal approach, and the state-of-the-art research and treatment facilities. The research institute employs more than 600 scientists investigating many aspects of cancer development, diagnosis, treatment and epidemiology. Scientists at the Netherlands Cancer Institute have excess to state-of-the-art research facilities supporting their basic, translational and clinical research. This scientific research could not be carried out without the institutional support of the Dutch Cancer Society, the Ministry of Health, Welfare and Sport, the many research grants obtained by our researchers from international funding agencies, and the generous donations made by individuals that support our research program. The Netherlands Cancer Institute is the only OECI designated Comprehensive Cancer Centre in the Netherlands. ***For more information visit our websites: www.nki.nl and www.avl.nl.***

Technical University of Munich

– Corporate Communications Centre

A safety switch that automatically stops the device for example before it overheats has been built into many electrical appliances. The body's cells are equipped with this kind of "emergency stop". They make sure that a defective cell does not grow uncontrollably to become transformed as a tumour cell. A team from the Technical University of Munich (TUM) has now discovered such a switch in immune T cells. In the future it will be possible to use these results in new therapies for the treatment of T cell non-Hodgkin's lymphoma triggered by defective immune cells.

In the body T cells are usually responsible for immediately detecting and killing cancer cells. However, problems can arise when a T cell itself develops a defect in its genome, the DNA. If the defect affects areas of the genome which are responsible for cell growth, referred to as oncogenes, the T cell itself can become an uncontrollably growing tumour cell. T cell, an important part of the body's immune system against cancer, can also fail.

This is exactly what occurs in T cell non-Hodgkin's lymphoma. This aggressive form of lymphoma has a very low rate of successful treatment and afflicts approximately one out of every 100,000 persons in Germany. Prof Jürgen Ruland, Director of the TUM Institute for Clinical Chemistry and Pathobiochemistry, and Principal Investigator at the TUM Central Institute for Translational Cancer Research (TranslaTUM) and the German Cancer Consortium (DKTK), is working together with his team to better understand the molecular mechanisms of these cancers to find ways of treating them more effectively.

PD-1 as the shut-off switch in tumour formation

In their study, currently published in "Nature", the scientists succeeded in a very important step by showing that the defective T cells also have an emergency shut-off switch, referred to as a tumour suppressor. They ascertained that the protein PD-1 can turn off defective T cells at an early stage and thus prevent them from becoming malignant. They discovered this function of PD-1 in a mouse model for T cell non-Hodgkin's lymphoma, and could also explain the mechanism. PD-1 is activated by defects in genes for cell growth, i.e. oncogenes, and then suppresses the effect of these genes using other proteins. Thus it functions as a shut-off switch to prevent the uncontrolled growth of defective T cells.

Tumour analysis helps in deciding the therapies that should be used

The scientists also successfully resolved the question of why many T cell non-Hodgkin's lymphomas are so aggressive, in spite of this protective function. They investigated genetic data sets from 150 patients: "Based on our previous results, we intentionally focused closely on PD-1. In individual groups of ›30 % of the patients showed changes in the regions of the genome that interfered with the production of PD-1. This has disastrous consequences in the tumour; PD-1 no longer functions as an 'emergency shut-off'. The diseased T cells can reproduce uncontrollably," explains Tim Wartewig, lead author of the study.

"These patients could be helped by medications that reverse the loss of PD-1 signalling and thereby destroy tumour cells. This type of medication already exists for other forms of cancer – in our opinion, use with T cell non-Hodgkin's lymphoma should also be considered," says Jürgen Ruland. The scientists therefore recommend investigating individual differences in tumours before making decisions about which medication is to be administered.

Original publication
T. Wartewig, Z. Kurgyis, S. Keppler, K. Pechloff, E. Hameister, R. Öllinger, R. Maresch, T. Buch, K. Steiger, C. Winter, R. Rad and J. Ruland, PD-1 is a haploinsufficient suppressor of T cell lymphomagenesis, Nature, November 2017, DOI: 10.1038/nature24649
https://www.nature.com/articles/nature24649

Contact: Prof. Dr. Jürgen Ruland, Institute for Clinical Chemistry and Pathbiochemistry, University Hospital TUM Klinikum rechts der Isar; E: jruland@lrz.tum.de T: +49 89 4140 4751.

Pancreatic cancer: specific protein promotes development of pancreatitis and tumours

Pancreatic cancer is one of the most aggressive forms of cancer and is currently very difficult to treat. However, the last few years have seen advances in the scientific understanding of how this cancer develops at a molecular level. For example, as well as certain risk factors, genetic changes also play a role. In a study published in leading journal "Cancer Cell", a team led by laboratory medicine specialist Jelena Todoric from MedUni Vienna's Institute of Laboratory Medicine and molecular biologist Michael Karin from the University of California in San Diego were able to show that disrupted cell autophagy can be a precursor for these genetic changes. This gives rise to an abnormal amount of the protein p62/SQSTM1, which negatively affects pancreatic cells and consequently causes the tissue changes that then progress into pancreatic cancer.

Approximately 1,500 people a year develop pancreatic cancer in Austria, accounting for around 4% of all malignant cancers. Initially, pancreatic cancer is virtually asymptomatic and that is why it is usually only diagnosed when it is well advanced. By this point fewer than 20% of patients are operable.

It is a known phenomenon in medical research that 16% of healthy people and 60% of patients suffering from pancreatitis, that is to say inflammation of the pancreas, exhibit so-called precursor lesions in the pancreas. There is a 1% probability that these might develop into cancer. However, genetic factors also play a role, as do risk factors such as smoking, obesity, diabetes and chronic pancreatitis. However, it was hitherto not understood how all these factors interrelate and what mechanisms lie behind them.

In a study using an animal model and human cell material, the team led by laboratory medicine specialist Jelena Todoric from MedUni Vienna's Institute of Laboratory Medicine and molecular biologist Michael Karin from the University of California in San Diego has now shown that a disruption to cell autophagy is involved in the development of pancreatic cancer. Autophagy is one of those

essential bodily processes whereby cells operate a form of recycling: breaking down and reutilising their own constituents and eliminating bad proteins and cellular waste. When the process is disrupted, for example due to smoking or obesity, this aggravates the existing genetic lesions on the pancreatic cells, the function of which is to produce digestive enzymes. This then results in an extraordinary accumulation of the protein p62/SQSTM1, which is typically elevated in chronic pancreatitis or in the precursor lesions (Pancreatic Intraepithelial Neoplasia PanIN).

The study showed that accumulation of p62/SQSTM1 promotes the development of early precursor lesions, so-called acinar ductal metaplasia. A subsequent cascade of molecular activities then go on to produce pancreatic cancer. In this process, the protein p62 first of all causes the displacement of a second protein known as NRF2 into the nucleus. This in turn stimulates production of the protein MDM2. Elevated MDM2 levels transform acinar cells, which exhibit certain carcinogenic gene mutations, into vigorously proliferating duct cells. This ultimately leads to the growth of the malignant pancreatic tumour, pancreatic ductal adenocarcinoma.

The results of the study suggest that a new therapeutic approach could be to treat autophagy, since most of the known risk factors disrupt this process. The development of targeted MDM2 medications could, in future, prevent the development of malignant pancreatic cancer in people with a high risk of the disease.

Medical University of Vienna

Medical University Vienna (MedUni Vienna) is one of the most traditional medical education and research facilities in Europe. With around 8,000 students, it is currently the largest medical training center in the German-speaking countries. With 5,500 employees, 27 university hospitals and three clinical institutes, 12 medical theory centres and numerous highly specialised laboratories, it is also one of Europe's leading research establishments in the biomedical sector.

Service: Cancer Cell: Stress Activated NRF2-MDM2 Cascade Controls Neoplastic Progression in Pancreas. Todoric J, Antonucci L, Di Caro G, Li N, Wu X, Lytle NK, Dhar D, Banerjee S, Fagman JB, Browne C, Umemura A, Valasek MA, Kessler H, Tarin D, Goggins M, Reya T, Diaz-Meco M, Moscat J, Karin M. Cancer Cell. 2017, in press. http://www.cell.com/cancer-cell/fulltext/S1535-6108(17)30464-6; DOI: http://dx.doi.org/10.1016/j.ccell.2017.10.011

Contact: Johannes Angerer,
Head of Communication and Public Relations,
Medical University of Vienna
Spitalgasse 23, 1090 Vienna
www.meduniwien.ac.at/pr
T: 43 (0)1 40 160 11 501
E: pr@meduniwien.ac.at

Postmenopausal breast cancer: sufficient to extend treatment by two years

– from the Medical University of Vienna – ABCSG study: 5+2 years is the optimum length of treatment with aromatase inhibitors

Standard treatment for postmenopausal breast cancer is to give a hormonal (endocrine) breast cancer drug for five years following surgical removal of the tumour. The results of the recent study (ABCSG 16/S.A.L.S.A) conducted by the Austrian Breast & Colorectal Cancer Study Group (ABCSG) now show that two years of follow-on treatment with the aromatase inhibitor anastrozole is sufficient. Further extension of treatment to five years is not helpful, because it does not improve the treatment outcome, but can worsen the side effects.

Anti-hormone therapy suppresses the female sex hormones oestrogen and/or progesterone, since they can stimulate the growth of hormone-receptor-positive tumours and thus lead to relapse (recurrence). Earlier studies suggested that extended endocrine therapy has a positive impact upon disease-free survival but the question of the optimum length of treatment has hitherto remained unanswered. ABCSG 16/S.A.L.S.A has now tested this important clinical question.

Seven or ten years of endocrine therapy?

A total of 3,484 postmenopausal breast cancer patients at more than 70 Austrian centres took part in the investigation between 2004 and 2010 – making it one of the largest clinical studies so far conducted in Austria. The participants had an early hormone-receptor-positive breast cancer (Stage I-III) and, after five years of standard adjuvant anti-hormone therapy (endocrine therapy) they received an additional two or five years of the aromatase inhibitor anastrozole by way of extended endocrine therapy. "We discovered that two years on an aromatase inhibitor following endocrine therapy are sufficient and that prolonging the treatment offers no benefit but increases side effects," says Michael Gnant, coordinating investigator for the study.

Clear results

Anastrozole blockades oestrogen synthesis, thereby preventing recurrence but has a different mode of action and a more favourable toxicity profile than tamoxifen, which has been used for many years. It has now been demonstrated in this and similarly designed international studies that patients do not benefit from extending endocrine therapy to five years but they do suffer more side effects, such as fractures. There is therefore no indication for a total treatment time of 10 years. Studies also show that patient compliance diminishes with longer treatment. "Up until now, we were unable to say whether there is a subgroup of patients that might benefit from extended treatment. We hope that the new molecular testing methods, which we are currently trialling, can bring more clarity in this respect," says Gnant, with an eye to the future.

Contact: Johannes Angerer
Head of Communication and Public Relations, Medical University of Vienna
Spitalgasse 23, 1090 Vienna
www.meduniwien.ac.at/pr
T: 43 (0)1 40 160 11 501
E: pr@meduniwien.ac.at

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 Denys Wheatley at Oncology News on E: editor@oncologynews.biz

Genomic Health (Redwood City, CA, USA)

Update on Cancer Treatment

The company reported at the 40th San Antonio Breast Cancer Symposium that new validation shows Oncotype DX breast recurrence score® test predicts clinical response to neoadjuvant hormonal therapy to improve surgical outcomes in certain patients with large tumours.

Analysing tumour biology with Oncotype DX can help guide treatment decisions prior to breast cancer surgery

Neoadjuvant systemic therapy, such as chemotherapy and hormonal therapy, can shrink tumour size and allow breast conserving surgery (BCS) for patients diagnosed with hormone receptor positive (HR+) large tumours (≥2cm), who may otherwise be advised to undergo a mastectomy. However, chemotherapy comes with its many debilitating side effects; in some patients, it does not improve surgical outcomes over hormonal therapy. Identifying patients whose tumours may not respond to chemotherapy using traditional parameters is difficult; as a result some patients receive chemotherapy treatment yet unfortunately derive no benefit.

Core needle biopsy samples from approximately 300 postmenopausal patients with HR+, HER2-, node-negative invasive breast cancer enrolled in the randomised Phase 3 NEOS study were analysed to determine clinical response to six months of hormonal therapy before surgery based on Recurrence Score® results. Analysis showed that Recurrence Score results are significantly associated with clinical response to hormonal neoadjuvant therapy ($p<0.001$). Specifically, findings suggest that, for patients with a score <18, treatment with neoadjuvant hormonal therapy alone could be an effective strategy. These patients might potentially avoid chemotherapy without reducing their chances of successful BCS. "This important validation study demonstrates that analysing tumour biology with Oncotype DX in the neoadjuvant setting can help guide treatment decisions," said Prof. Hiroji Iwata, Principal Study Investigator, Department of Breast Oncology, Aichi Cancer Center Hospital, Nagoya, Japan. "In particular, patients with a low Recurrence Score result tend to have higher clinical response rate with neoadjuvant hormonal therapy, which makes it possible to shrink the tumour size and achieve breast conserving surgery leading to better cosmetic outcomes whilst limiting the impact of treatment side effects on their quality of life."

New results from large registry with ten-year follow up show excellent outcomes for patients with low Recurrence Score results treated with hormonal therapy alone

In a study from Clalit Health Services, the largest health services organisation in Israel, medical records of >1,500 patients with node-negative breast cancer or with micro-metastases tested between January 2006 and December 2009 were examined to verify given treatment and subsequent outcomes. Use of chemotherapy was aligned with Recurrence Score results. Patients who had been diagnosed with HR+, node-negative breast cancer, and who had Recurrence Scores of <18,most of whom (98.2%, 632) were treated with hormonal therapy alone, had excellent outcomes, with 10-year Kaplan Meier estimates of distant recurrence (3.9%) and breast cancer specific survival rate (98.1%). "This important analysis with long-term follow-up shows that patients with low Recurrence Score results can be treated with hormonal therapy alone and indicates that withholding chemotherapy is possible in those with intermediate risk and Recurrence Score results up to 25. The genomic information provided by the Oncotype DX test is important in order to identify patients who can be spared the toxicity of chemotherapy." (Prof. Salomon Stemmer, Lead investigator of the study, Department of Oncology, Davidoff Center, Rabin Medical Center affiliated to Tel Aviv University, Israel.)

New data reinforce specific value of examining tumour biology with Oncotype DX in older women

The prospective West German Study Group's (WSG) Plan B trial examined Oncotype DX Breast Recurrence Score results in patients aged 70 years and over versus those under 70. For patients with higher risk tumours (Recurrence Score result >25) treated with chemotherapy, results showed comparable disease-free survival rates regardless of which age bracket they fell. The findings reinforce the value of the Oncotype DX Breast Recurrence Score test for older patients to identify more accurately those who would derive benefit from chemotherapy.

Seattle Genetics and Bristol-Myers Squibb – Cancer Update

At the American Society of Hematology Annual Meeting, 2017, in Atlanta, Georgia, the companies have announced updated safety and efficacy data from an ongoing phase 1/2 clinical trial evaluating ADCETRIS in combination with Opdivo in relapsed or refractory classical Hodgkin lymphoma. Their studies have shown the following:

1. 83% of response-evaluable patients (n=60) had an objective response, including 62 and 22% of the patients experiencing a complete response and partial response, respectively.
2. The estimated 6-month progression-free survival rate was 89%.
3. Preliminary analysis suggests combination treatment with ADCETRIS and Opdivo on stem cell mobilisation or engraftment is unaffected.

Agendia Inc – Recent Reports

Key Studies were presented at the San Antonio Breast Cancer Symposium (December 2017 demonstrate the important role of MammaPrint® for patient pre-selection, cost-effectiveness and for younger patients. I-SPY 2 is a phase II neoadjuvant clinical trial designed to decrease the amount of time required to collect drug efficacy data. The first long-term survival results from trial for patients pre-selected by MammaPrint were presented.

The results support the use of pathological complete response (pCR) as a primary endpoint for accelerated approval of new drugs Data from the I-SPY 2 trial showed the first long-term survival results for patients pre-selected as MammaPrint high-risk, with 94% of the patients who achieved pathological complete response event-free at three years. The company also showed that MammaPrint assessment is cost effective in clinical high risk patients compared to clinical risk assessment alone. The product is an in vitro diagnostic medical device, performed in a central laboratory, using the gene expression profile of breast cancer tissue samples to assess a patients' risk for distant metastasis.

Achieving pCR was a strong surrogate endpoint for improved Event Free Survival (EFS) and Distant Disease-Free Survival (DDFS) across all 11 treatment arms, regardless of molecular subtype. Patients who achieved pCR had an impressive three-year EFS and DDFS of 94% and 95% respectively. Based on these findings, the I-SPY2 TRIAL will now test whether therapy can be de-escalated or escalated for individual patients with the goal of achieving pCR for all.

Additional data from the MINDACT trial showed that not all young women with breast cancer are at high risk of disease recurrence. MammaPrint classified 48% of the 1,100 patients as genomic High Risk, compared to 61% using clinical risk assessment alone. The outcome for women with a MammaPrint Low Risk result within the three age categories of up to 45, 45-55 and 55 or over, was a five-year Distant Metastasis-Free Survival (DMFS) of 95-98%. These clinically-relevant results add important additional data to limited available evidence on genomic expression in young early-stage breast cancer patients.

Dr. William Audeh, Chief Medical Officer at Agendia, said: "We are seeing the utility of using MammaPrint to pre-select patients for the I-SPY 2 trial in the shape of the impressive first long-term survival outcomes, plus encouraging cost-effectiveness data to support the level 1A evidence already proving the clinical benefits of the test." "The continuing value of the unique and independent MINDACT … will enable physicians to better support younger patients with breast cancer and tailor treatment based on genomic risk-of-recurrence, a group for whom further evidence was certainly needed."

To have your event listed in the Oncology News diary,
E: info@oncologynews.biz

2018

January

BTOG 2018 – 16th Annual BTOG Conference 2018
24-26 January 2018; Dublin, Ireland
BTOG , T: + 44 (0)116 250 2811, E: dawn.mckinley@btog.org
W: www.btog.org
@BTOGORG

February

Treatment advances in Haemato-oncology
19 February 2018; London, UK
E: conferenceteam@rmh.nhs.uk
T: +44 (0)20 7808 2921
W: www.royalmarsden.nhs.uk/studydays
@trmeducation

March

Neuro-oncology Conference
8 March 2018; London, UK
T: +44 (0)20 7808 2921, E: conferenceteam@rmh.nhs.uk
W: www.royalmarsden.nhs.uk/studydays
@trmeducation

5th Symposium on Molecular Pathology in Oncology
15 March 2018; London, UK
T: +44 (0)20 7808 2921, E: conferenceteam@rmh.nhs.uk
W: www.royalmarsden.nhs.uk/studydays
@trmeducation

June

International Symposium in Paediatric Neuro-oncology
29 June – 3 July 2018; Denver, USA
W: ISPNO2018.org

Cancer and Bone Society (CABS) 2018 Meeting, jointly with the 8th International Workshop on Advances in the Molecular Pharmacology and Therapeutics of Bone and other Musculoskeletal Diseases
30 June – 3 July 2018; Oxford, UK
W: www.molpharmworkshop.org

October

EANO 2018
11-14 October 2018; Stockholm, Sweden
W: www.eano.eu

ESMO 2018 Congress
19-23 October 2018; Munich, Germany
W: esmo.org

November

SIOP 2018 Annual Meeting
16-19 November 2018; Kyoto, Japan
E: siopoffice@kenes.com
W: http://siop-online.org/event/siop-2018

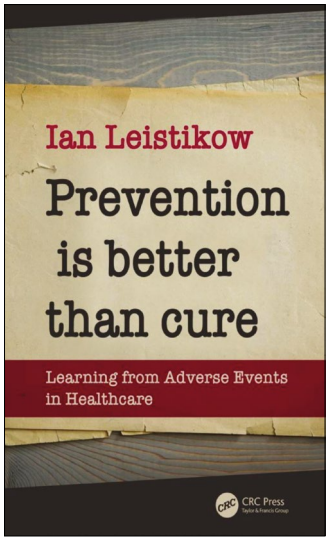
2019

September

EANO 2019
18-22 September 2019; Lyon, France
W: www.eano.eu

Prevention is Better Than Cure
Learning from adverse events in healthcare

Author: Ian Leistikow. Published by: CRC Press, Taylor & Francis Group, Boca Raton, FL, 2017. ISBN: 978-1138197763



In the course of his career, the author has ended up as a Senior Inspector in The Dutch Healthcare Inspectorate, making him suitably qualified to address the subject. The focus is firmly on patient safety, or more precisely on cases in which patient safety has been compromised because of the lack of proper care at different levels throughout the medical profession. He espouses that too little attention is paid to this problem, probably arising because there seems to be inadequate training in this respect.

In the dozen cases dealt with in some detail, most can be put down to human error which has meant that patients have suffered worse than is acceptable, and in most cases this could have been prevented. If it is argued that a single case is one too many, it can also be argued that in any job or profession avoidable errors could have been prevented ("to err is human"). What is not made clear is whether errors are more endemic in healthcare than in other profession. He does admit, however, in his Epilogue that "far, far more often things go right".

My concern about this book is in its main title, since the content deals with matter better summed up in the subtitle, since it seems addresses more accurately the issue that taking the right decisions early on can ensure that disease and disorder can be avoided. Prevention in these times is seen as a priority, but the cases covered in this book are individual errors due to such problems as tiredness, misdiagnosis, making wrong assumptions, inappropriate treatment through haste and inexperience among others. In some cases the follow-up has been poor. As far as oncologists are concerned, there is virtually no mention of cases in this field of medicine, where prevention is in recognising the hazards of such carcinogens as asbestos, benzpyrene in tobacco tar and HPV. The main title again would indeed be more pertinent to a volume on cancer prevention. In the Epilogue again there is one mention of cancer; in the Netherland over a period of four to five years between 2007 and 2012, mortality following cancer surgery has fallen by 25%, but no explanation is offered! Has this anything to do with inadequate training or improved procedures? While the message in the book can be relevant to all medics, it seems common sense and alertness were lacking in many instances. One chapter sums up the basic problem, being appropriately entitled "Assumption is the mother of all screw-ups".

Honour for cancer professor at university of Leicester and Leicester's hospitals

Professor Mick Peake recognised for lifelong work in cancer research and care

At the University of Leicester, Professor and consultant at Leicester's Hospitals has been honoured for his lifelong work on earlier diagnosis and improvement of outcomes of lung cancer patients. The award by the Irish Cancer Society followed the Charles Cully Memorial Lecture. The lecture recognises and awards leadership in the fields of cancer control, cancer prevention and health policy, and provides an opportunity to highlight best practice or innovation in those areas.

The Irish Cancer Society has commissioned research from the National Cancer Registry of Ireland to establish the proportion of cancers diagnosed via emergency presentation across the top ten cancers. Preliminary findings of this important research were launched at this year's Annual Charles Cully Memorial Lecture.

Professor Peake's lecture, 'Towards the earlier diagnosis and improved outcomes of lung cancer patients' focussed on:

- optimising the early diagnosis of lung cancer
- national and international statistics around survival and late diagnosis
- the experience and impact of the public awareness campaigns
- the scale and problem of emergency presentations
- efforts to promote the optimisation of the lung cancer care pathway

"It was a great honour to receive The Charles Cully medal at the annual meeting of the Irish Cancer Society. I was speaking about the huge progress that we had made in the quality of care, earlier diagnosis and outcomes for lung cancer patients in the UK over the last 15 years or so. A significant amount of this came from my work leading the establishment of the Thoracic Oncology Unit in the University Hospitals of Leicester, but I have been extremely fortunate to work with a great range of clinicians and researchers over the years in which I have often only been the 'front man', so my thanks go out to all my colleagues over the years. Ireland is looking to implement their recent National Cancer Strategy 2017-2026, and I hope that the work demonstrated in my lecture may have given food for thought as to how some of the initiatives outlined in that plan might be taken forward."

Professor Peake pictured with the Irish Cancer Society's Head of Services and Advocacy Donal Buggy and CEO John McCormack.

Donal Buggy, Head of Services and Advocacy at the Irish Cancer Society, said: "We are delighted to honour Professor Peake with the Charles Cully Medal 2017, for all the work he has done championing the earlier diagnosis of lung cancer. "He has worked tirelessly on this issue throughout his career, driving the issue of lung cancer up the political agenda. Without a doubt lung cancer services in the UK would not be where they are today without Professor Mick Peake,and we are delighted he could come and share his expertise and insights with us."

Professor Peake is the Clinical Lead for Early Diagnosis in Public Health England's National Cancer Registration and Analysis Service, where he oversees the clinical understanding and analysis of UK-wide population data on cancer. He has had a major interest in lung cancer and mesothelioma for many years. He was Clinical Lead for the National Lung Cancer Audit in the Royal College of Physicians, where he was Associate Director of the Clinical Effectiveness and Evaluation Unit for 20 years. He was National Clinical Lead for Lung Cancer and for NHS Cancer Improvement until the dissolution of the organisation in the NHS reforms. Amongst other roles he is a member of the board of trustees of the British Thoracic Oncology Group, chair of Mesothelioma UK, the National Lung Cancer Forum for Nurses and also Chairs the Clinical Advisory Group of the UK Lung Cancer Coalition.He has been involved in the development and implementation of national cancer policy since the late 1990s and has published widely, his major interests being in early diagnosis and improving outcomes for cancer patients by proper service configuration, supported by good clinical outcome data.

For more information contact Professor Mick Peake: mick.peake@uhl-tr.nhs.uk or mick.peake@phe.gov.uk

Association of Community Cancer Centres Honoured Medical Oncologist and AMA President-Elect Barbara L. McAneny with National Award

Achievements in Practice Transformation Take Centre Stage at 34th National Oncology Conference, Rockville, Maryland - October 26, 2017

In recognition of her pioneering work in value-based care, Barbara McAneny, MD, FASCO, MACP, was honoured with the Annual Achievement Award of the Association of Community Cancer Centres (ACCC). Her ground-breaking work in developing the grant-funded COME HOME oncology medical home initiative reduced costs and improved care, helped to inform Medicare's current Oncology Care Model (OCM) pilot, and supported physician practices in process changes critical to participation in value-based payment models, including those created under the Medicare Access and CHIP Reauthorization Act (MACRA). This is a year of honours for Dr McAneny, a board-certified medical oncologist/hematologist from Albuquerque, New Mexico, who in June became the first oncologist to be voted president-elect of the American Medical Association (AMA). She will assume the presidency in June 2018.

The ACCC Annual Achievement Award recognises individuals who have made outstanding contributions nationally and/or internationally to cancer care and patients. Past honorees include esteemed cancer advocates and foundation leaders, as well as U.S. presidents and senators, such as President Richard M Nixon, President George HW Bush, and Senator Ted Kennedy.

Dr McAneny received the Annual Achievement Award before approximately 800 attendees at the ACCC National Oncology Conference held October 18-20 in Nashville, Tennessee. Dr McAneny's acceptance speech conveyed her unique perspective as a physician who successfully transitioned to a leadership role within the nation's rapidly evolving healthcare environment. "It is a great honour to receive this ACCC award,"… "This is an organisation that brings together thousands of specialists from all areas of cancer care, from cancer centres and hospitals to private practices and academic centres. All of us have a common cause, which is taking care of cancer patients. So, to receive an award from an organisation that has so many great people to choose from is one of the greatest honours of my life!"

From left to right: ACCC President-Elect Thomas A. Gallo, MS; ACCC Immediate Past President Jennie R. Crews, MD, MMM, FACP; Barbara L. McAneny, MD, FASCO, MACP; and ACCC President Mark S. Soberman, MD, MBA, FACS.

Dr McAneny also emphasised the AMA's a long-standing principle of increasing access to healthcare through insurance coverage which is she said "…especially important for cancer patients." Reflecting on evolving practice transformation, she urged alignment between practice delivery models and newly emerging payment models. "A medical home isn't a payment methodology, it's a practice methodology," she said. We need a payment model that works with it." It is needed "because our country can't afford to lose the infrastructure of cancer care." As AMA President-Elect, she hopes Congress will work with doctors across America to fix our ailing healthcare system so that every individual with cancer can get the care he or she deserves.

About the Association of Community Cancer Centres

The Association of Community Cancer Centres (ACCC) is the leading advocacy and education organisation for the multidisciplinary cancer care team. More than 23,000 cancer care professionals from over 2,500 hospitals and practices nationwide are affiliated with ACCC. Providing a national forum for addressing issues that affect community cancer programs, ACCC is recognised as the premier provider of resources for the entire oncology care team. Our members include medical and radiation oncologists, surgeons, cancer program administrators and medical directors, senior hospital executives, practice managers, pharmacists, oncology nurses, radiation therapists, social workers, and cancer program data managers. For more information, visit ACCC's website at www.accc-cancer.org. Follow us on Facebook, Twitter, LinkedIn, and read our blog, ACCCBuzz.

ACCC contact:
Lori Gardner
Senior Director,
Communications & Marketing
Tel:+1-301-984-9496 ext. 226

Kings College Hospital – New Appointment

The first clinical nurse specialist is to focus on quality of life for brain tumour patients

The Neuro-Oncology team at King's College Hospital is pleased to welcome Charlotte Robinson into the first funded low-grade glioma Clinical Nurse Specialist (CNS) post in the UK, sponsored by The Brain Tumour Charity. Charlotte brings four years of oncology and surgical experience with her which will give her appropriate insight to working with this patient group.

Charlotte attended the Teenage and Young Adult one-stop clinic at Guy's Hospital in October, 2017, whose largest cohort of patients is from neuro-oncology; she is really excited about getting involved with this group of particularly vulnerable patients. She hopes to develop a service where a holistic support network is established which caters for all of patient's holistic needs. Charlotte said: "I want to do all I can to be there for patients with low grade brain tumours – whether that is with advice on symptom management or emotional support and someone to talk to. I'm really excited about what potential this role has for patients and hope to make their experience as straightforward as possible."

Her appointment marks a landmark development in The Charity's drive to improve the quality of life care for all those affected by this devastating disease and its own research has shown the benefits of having such a one point of contact throughout their treatment and aftercare.In The Charity's report Finding Myself in your Hands: The Reality of Brain Treatment and Care (2016) only 53% of people diagnosed with a low grade tumour said that they had access to this single point of contact. This compared to 76% of those diagnosed with a high grade brain tumour.

When people do have access to a clinical nurse specialist, 74% say they

are satisfied with the care they provide. However, those without a CNS or other single point of contact were:

- 1.5 times more likely to report a high symptom burden (43.6% compared with 29.1%)
- 1.6 times more likely to say that their brain tumour had severely affected their emotional or mental health (30.7% compared with 19.6%)
- 2.7 times more likely to disagree they had good access to information on managing symptoms (46.1% compared with 17.1%)
- 4.7 times more likely to disagree that that the healthcare professionals they dealt with understood brain tumours (44% compared with 9.4%)

Prof Keyoumars Ashkan, Department of Neurosurgery, Kings College Hospital said: "Our partnership with The Brain Tumour Charity to appoint Charlotte as UK's first charity funded Low Grade Glioma Clinical Nurse Specialist underpins our joint commitment to improve the care of this group of patients. The unmet need to address the holistic care of these patients is an area of high priority and this appointment will go a long way to progress our neuro-oncology service in general and the Low Grade Glioma service in particular in the quest to meet these challenges."

"This unique development is a witness to the shared ethos and vision of The Brain Tumour Charity and the King's Health Partners to provide world class care for our patients."

Emma Tingley, Director of Services and Influencing, said: "We are committed to having the biggest possible impact for everyone affected by a brain tumour in the UK and are delighted to be funding our first Clinical Nurse Specialist in partnership with Kings College Hospital. For those diagnosed with a low grade tumour who live with the sustained and significant consequences and impact of this, they often miss out even on the essential services because they have not been given a cancer diagnosis. This first Clinical Nurse Specialist post will focus on providing a dedicated service to those diagnosed with a low grade brain tumour. Having a single point of contact from diagnosis is essential in reducing the burden of symptoms, including the emotional and mental health difficulties that often result from the diagnosis."

For further information and media enquiries please contact: Piers Townley, PR and Media Officer, The Brain Tumour Charity. DD: 01252 749991. Mob: 07990 828385, piers.townley@thebraintumourcharity.org

Her appointment marks a landmark development in The Charity's drive to improve the quality of life care for all those affected by this devastating disease

Latest developments on products and services from the industry. To have your news included contact Denys Wheatley at Oncology News, E: editor@oncologynews.biz

Paxman Scalp Cooling named in Cleveland Clinic's top 10 Medical Innovations for 2018

Paxman Scalp Cooling System has been named as one of Cleveland Clinic's Top 10 Medical Innovations of 2018. The list of up-and-coming technologies, selected by a panel of Cleveland Clinic physicians and scientists, was announced at a presentation at the 2017 Medical Innovation Summit. Now in its 15th year, the annual Medical Innovation Summit is organised by Cleveland Clinic Innovations, the development and commercialisation arm of Cleveland Clinic.

Speaking about the announcement, CEO of Paxman, Richard Paxman said: "We are delighted to have been named as one of the top medical innovations of 2018. My team have worked so hard to develop a system that helps women retain their hair and gives them an alternative to chemotherapy-induced hair loss. I am so proud that all our hard work, research and determination have been recognised in such a prestigious way by the Cleveland Clinic." The report highlights that 'newly diagnosed' cancer patients have a lot to process, and for women the inevitable loss of hair is often one of the hardest side effects. The Paxman Scalp Cooler is a new technology that is on its way to the U.S. to help eliminate this problem from some of the worries of patient.

Scalp cooling reducing the temperature by

a few degrees immediately before, during and after chemotherapy. It is effective in preserving hair of women receiving chemotherapy for early-stage breast cancer.

Developed in Huddersfield, UK, the system is the world-leading hair loss prevention system for chemotherapy patients. It has been used by over 100,000 patients in 32 countries; it is responsible for helping patients to keep their hair and retain normality during chemotherapy. The system was US cleared by the Food and Drug Administration (FDA) in May 2017.

Chemotherapy works by targeting rapidly dividing cells in the body, but the epithelium generating hair has the second fastest dividers; their damage and death in hair follicles during chemotherapy leads to alopecia approximately two weeks after the commencement of treatment.

Used all over the world, the Paxman Scalp Cooling System is available in two models. The single model provides cooling for one patient and is suitable for a small chemotherapy suite or private bed, whilst the double system provides cooling for one or two patients simultaneously with each cap working independently. Made from lightweight, silicone, the scalp cooling cap is soft and flexible – providing a snug yet comfortable cap during treatment. Molding to all head shapes and sizes, liquid coolant passes through the cap, exchanging heat from the patient's scalp, ensuring it remains at a constant temperature to minimise hair loss. Backed by leading oncologists from around the world, the system has achieved global success in many hospitals and specialist cancer treatment centres.

For more information or to request an interview with Paxman, please contact Julia Price, E: julia@juliaprice.co.uk T: +44 (0)7737 864878.

Agilent Technologies Leading lung cancer experts on the role of pathologists in care-teams and advancing precision medicine

A short film by Agilent Technologies – A New Frontier in the Fight Against Cancer – explores the increasing role of laboratory diagnostics and specialist care-teams in the age of personalised/precision medicine. In the film, leading lung cancer specialists including Dr Roy Herbst from (Yale Cancer Center) and Dr. Phillipe Taniere from (Queen Elizabeth Hospital, Birmingham), among other leading pathology figures, comment on the heightened importance of pathologists in advancing the diagnosis and treatment of lung cancer. According to experts, this shifting landscape has brought pathologists using more molecular approaches closer to playing an integral part of a patient's care-team. Some 60-70% of healthcare decisions are now based on a test results from them. This information can also potentially reduce healthcare costs by as much as $28,000 per person in the US, and improve care quality by reducing unnecessary treatments.

[Agilent is a worldwide leader in partnering with pharmaceutical companies to develop immunohistochemical-based diagnostics for cancer therapy. For over 20 years, Agilent scientists have been focusing on the development of personalised medicine, which is where Agilent's Dako brand of diagnostics comes into play, providing important information about the status of key biomarkers in individual cancer patients. It is partnered with Merck.]

Ending the Isolation: A Guide to Developing National Rare Cancers Networks

Rare cancers account for 22% of all diagnosed cancer cases. But clinicians may see some types just once in a lifetime, and patients desperately need expertise and experience in diagnosis and treatment. A European Commission-backed project is now underway to improve patient survival by pooling expertise internationally in European Reference Networks.

- But can such European initiatives work without national networks of expertise already in place?
- What sort of national structures and initiatives are required to address rare cancers?
- Are countries leading the way on rare cancers in danger of being overburdened by European Reference Networks?

In this essay, Simon Crompton examines what needs to happen if people with rare cancers are to receive quality care throughout Europe.

You can read this article at Cancer World online. [Editor's comment – it seems odd that "rare" cancers constitute over one fifth of all cancers. Since classification of tumours is not a rigid exercise, truly rare cancers would be fewer. This also does

New resource to challenge widespread poor practice in biomedical research on the use of chemical probes

From The Institute of Cancer Research (ICR), London (http://www.icr.ac.uk)

"Many chemical probes used in biomedical research and drug discovery fail to meet quality criteria; the New Probe Miner resource helps researchers identify good, bad and ugly chemical tools"

A major new online resource designed to improve biomedical research by helping researchers choose the best chemical probes for their experiments – allowing drug targets to be validated much more effectively – has been launched. Chemical probes (aka "tools") are small molecules that scientists use to understand how individual proteins function, both in healthy cells and in diseases such as cancer. Scientists created the new resource after analysing almost two million chemical compounds that could be used to test the effects of inactivating a specific protein in cells – and finding that many were inadequate for the job. Researchers across the world are using chemical probes that lack specificity for a single drug target and are often so broadly promiscuous that they are incapable of yielding any useful data. There are worrying implications for the reliability of many published studies.

Biological researchers may often be unware of some the limitations of certain chemical probes, employing search engines or commercial catalogues that fail to discriminate between high-quality probes and those that are badly flawed or out of date. Probe Miner, a publicly available, free-to-use web-based resource, was created by scientists at The Institute of Cancer Research, London, and is the one of the first large-scale objective resources on chemical probes. It scrutinises data on more than 1.8 million chemical compounds for their suitability as probes against 2,220 human proteins and potential drug targets – selecting what seems to be acceptable from those that fail to meet its standard. Probe Miner is used to rank objectively chemical compounds – employing criteria for quality that include potency, selectivity and cell permeability. It gives lower rankings to the less suitable and unsuitable probes – e.g. those that hit several targets at once, and others that have indiscriminate and promiscuous activity against very many targets, respectively. Using the Probe Miner resource, the researchers concluded that only 250 human targets (1.2% of human proteins) are sufficiently effective and reliable to be used in research applications.

These chemical probes play a crucial role in discovering new drugs – by demonstrating, or 'validating', that the function of a protein target is important in disease and also by acting as prototype drugs to show that it is technically possible to inactivate the target of interest with a small molecule. But not all claimed chemical probes are of the same quality, and biomedical researchers need better information to avoid selecting flawed or out-of-date probes for their research. The new Probe Miner database allows researchers to search and rank the best chemical probes to help them find the answer to the scientific question of interest, thereby increasing the robustness of experimental findings and reducing waste of resources. ICR researchers uncovered a vicious cycle where scientists might find a weak probe on a search engine, use it in their research and publish their results, which then increases the likelihood of that probe is found by others through search engines, perpetuating the cycle. This could potentially weaken the use of better probes as they drop rank in web searches, weakening the stronger. Probe Miner, however, objectively scrutinises over 200 million experimental measurements to overcome this bias, and should become more effective as more data become available on better but "under-studied" probes. It has been estimated that spending £150 on a flawed chemical probe can cost the scientific community billions of pounds in wasted time and effort – and can delay the discovery and development for patients of innovative cancer drugs (published in Cell Chemical Biology).

The Probe Miner project has been funded by the European Union, the Wellcome Trust, Cancer Research UK in association with ICR.

Dr Bissan Al-Lazikani, Co-creator of Probe Miner and Head of Data Science at The Institute of Cancer Research, London, said: "Good chemical probes play a vital role in biomedical research – helping scientists to specifically switch off the functions of proteins of interest within cells, to precisely understand the jobs carried out by different proteins. But too many of the probes used in research are not of good quality, do not hit protein targets specifically, and end up producing misleading scientific results. Biomedical researchers often lack the information they need to select suitable probes and are stuck with no accessible way to evaluate them. Yet on the other hand, we have tens of millions of published experimental measurements that can help – if only researchers had a way to navigate through them.

Co-creator Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said: "The field of biomedical research has a very serious problem with chemical probes – contributing to the current crisis in reproducibility and robustness. A high proportion of chemical compounds claimed as useful probes in fact hit multiple targets at once, and some are frankly disastrous – producing results which can be highly misleading or plain wrong. There are many so-called probes still in use that are now well known to experts to be deeply flawed, and yet have been applied in literally millions of publications worldwide and continue to be employed today. Our new Probe Miner resource provides biomedical scientists with detailed, up-to-date information about all chemical tools available, so they can make informed decisions about which ones are the best fit for their research. We hope this will make the results of research more correct and robust while reducing waste – of time and money. I would urge all biomedical researchers to ensure that the probes they are using are up to the job – because otherwise their science will suffer, vital drug discovery research will be suspect, and progress to patient benefit will be delayed. We were disappointed to find such a low number of quality chemical tools available to study human proteins and to see so many examples of poor practice. It is vital that we encourage the research community to continue to develop new chemical probes, if we are ever to move away from well-studied drug targets and truly innovate in drug discovery. But the probes we use must be of sufficient quality and fit for purpose or science and patients will pay the price. We think Probe Miner will be a big help."

[Probe Miner is designed to complement the expert-curated database Chemical Probes Portal by providing large-scale, objective, data-driven information that will be continuously updated to keep track of fast-moving advances in the field. The researchers stress that the synergistic nature of the two resources makes their use in combination especially powerful for selecting the best chemical probes. This is aided by easy-to-use links between the two resources.]

Probe Miner is freely available at probeminer.icr.ac.uk

For more information please contact Ben Kolb in the ICR press office on 020 7153 5359 or ben.kolb@icr.ac.uk.

Final Appraisal Determination (FAD) appeal by Pfzer of inotuzumab ozo-gamicin

Pfizer announced on 28th December 2017 that its appeal has been upheld against the National Institute for Health and Care Excellence's (NICE) decision not to recommend BESPONSA® (inotuzumab ozogamicin) as a treatment for adults with relapsed or refractory (R/R) CD22-positive B-cell precursor acute lymphoblastic leukaemia (ALL). The NICE appraisal committee will now re-assess the evidence for inotuzumab ozogamicin before issuing a second Final Appraisal Determination (FAD).

Inotuzumab ozogamicin is an antibody drug conjugate approved by the European Medicines Agency (EMA) for patients with Philadelphia chromosome positive (Ph+) and Philadelphia chromosome negative (Ph-) relapsed or refractory CD22-positive B-cell ALL. It is a medicine that could fulfill significant unmet needs for patients with relapsed or refractory ALL, particularly those with Ph+ disease.

ALL is an aggressive type of leukaemia that can be fatal within a matter of months if left untreated. It is a rare disease, with around 760 people in the UK being diagnosed every year. The goal of treatment in relapsed or refractory ALL is to achieve complete remission and enable the patient to have a potentially curative stem cell transplant.[vi] Currently, there are few treatment options that can achieve complete remission, and patients have a very poor prognosis. In adult patients with R/R ALL, median overall survival is just three to six months.

Inotuzumab ozogamicin is an antibody drug conjugate comprised of a monoclonal antibody targeting CD22, a cell surface antigen expressed on cancer cells in almost all B-ALL patients, linked to a cytotoxic agent. When inotuzumab ozogamicin binds to the CD22 antigen on B-cells, it is internalised by the cell, where the cytotoxic agent, calicheamicin, is released to destroy the cell. The drug is administered by iv over one hour, providing patients with the option to be treated as outpatients for one hour a week, thereby potentially helping to alleviate hospital pressures and improve quality of life for patients.

GCI Health Pfizer Team
Tel: 0207 072 4211 Email: laura.andre@gcihealth.com

Pfizer Press Office
Tel: 0845 300 8033
Email: PressofficeUK@pfizer.com

Op-Ed: Recognising patients on World Clinical Trials Day

Dr Catherine Taylor, Haematology Therapy Area Lead, Janssen EMEA

At Janssen, our goal is a world without cancer and we are proud to celebrate World Clinical Trials Day to recognise the vital role that patients play in the progress towards finding better treatments for cancer. When it comes to treatments for cancer, science advances all the time, so we need the continuing goodwill of patients to take part in studies to show how these new medicines work, compared to existing treatments.

In 2014, there were 356,860 new cases of cancer in the UK and 163,444 deaths [1]; cancer is now the second leading cause of premature death in Europe [2]. Clinical cancer trials have helped pharmaceutical companies contribute to improvements in overall survival rates, earlier detection rates, ways of lowering the risk of getting cancer, in investigating approaches such as disease interception – a process that helps stop cancer before it can get a hold in the body – and to develop treatments with fewer side effects. However, one of the biggest challenges the industry is facing is that we are not getting enough people into these vital clinical trials – only 20 percent of cancer patients are in clinical trials, so while taking into account that not everyone is eligible, there is room for improvement in participation rates.

There is understandable anxiety among people who have just been told they have a frightening disease about being treated with a medicine under development. Many people just want to stick with what has already been tried and tested. But to make progress in fighting cancer, we need more people to step forward to help eliminate the disease by newer interventions. Many potential trial participants do not realise how heavily regulated clinical trials are. Laws are in place, such as the European Clinical Trials Directives, that give very clear guidelines on what is and what is not permitted. Clinical trials are thoroughly scrutinised by the European Medicines Agency, as well as ethics committees. Before you are allowed to embark on studies that offer a new treatment in comparison to current standard of care, you have to show very clear clinical evidence that this is going to be equal to or better than the current standard of care, and will not do harm to patients.

We have made so many advances in cancer thanks to people who have been willing to be involved in trials. It is important that people keep an open mind and not see it as something else to worry about that could cause stress. The ethos in clinical trials is always that the patient should never lose out. You would never knowingly be given an inferior treatment because this would be unethical. We are committed to allaying the fears and misconceptions of potential trial patients. It is important that people are well-informed about the reasons they need to consider in becoming involved. We want to put patients at ease when asking questions before they agree, and to make sure they can withdraw at any point without having to justify themselves. It is made very clear what the aims of the clinical trial are, and what treatments are being compared. We explain why the new treatment could offer benefits and what has been previously found in earlier studies. Potential patients are given the relevant they need at the level they can cope with, and allow them the time to digest and understand. This balance can be really hard because often there is not the luxury of having any delay in the cancer treatment. This makes it important that potential patients do not feel rushed or pressurised into making a decision. To help more patients to be informed, Janssen has set up a clinical trials finder website, www.globaltrialfinder.janssen.com, where patients can search according to their location and condition. Using the site, people can find out what trials are being carried out at hospitals and clinics near them and, if they wish, learn more about these trials. Clear, simple-to-find information and transparency in how the data collected in the trial will be used is the first step in helping people make a decision whether to participate.

Like most scientists working in this field, we are eager that as many people as possible can benefit from our clinical trials. That is why we are proud to be working in collaboration with Yale University on their YODA (Yale School of Medicine's Open Data Access) Project to allow scientists across the globe to gain access to our trial data. We want to encourage the sharing of data and discoveries and foster cooperation in order to get to the point where we not only fight cancer, but move towards eradicating it. To do this, we have started a World Without Cancer Research and Development Unit to show our commitment.

At Janssen Oncology, we dedicate ourselves to doing everything possible to improve lives and enable those affected by cancer to enjoy more of life's meaningful moments. We could not have come this far without the help of all the thousands of patients who have participated in clinical trials. They should be extremely proud of the contribution they have made in the fight against cancer.

References

1. Figure source for UK stats: Cancer Research UK: go to http://www.cancerresearchuk.org/health-professional/cancer-statistics
2. Figure source for European stats: World Health Organization: go to http://www.euro.who.int/__data/assets/pdf_file/0004/197113/EHR2012-Eng.pdf

Varian announces a new advanced cancer treatment system now available to cancer centres in Brazil

Further expanding the global availability of its new device for cancer treatment, Varian (NYSE: VAR) reports that the Halcyon™ system has received ANVISA registration in Brazil. This registration allows Varian to market this new system in Brazil. Halcyon simplifies and enhances virtually every aspect of image-guided volumetric intensity modulated radiotherapy (IMRT), and is well suited to treat a majority of cancer patients, offering advanced treatments for prostate, breast, head & neck, and many other forms of cancer.

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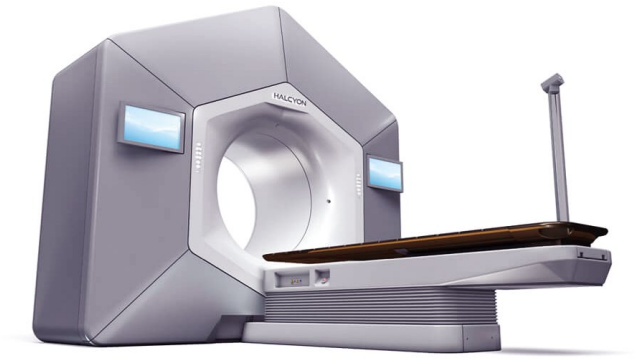
"Halcyon is engineered to revolutionise the clinical workflow and advance cost-effective cancer care worldwide," said Kolleen Kennedy, president of Varian's Oncology Systems business. "With ANVISA registration, clinicians in Brazil now have access to this new technology and we look forward to continuing our close collaboration with them in the global fight against cancer."

Halcyon is an advanced system that was designed to improve patient comfort, simplify operations, and shorten the time from installation to first-treatment without sacrificing quality. Patients benefit from its quiet operating environment, which is up to 2x quieter than other systems. Additionally, Halcyon has a low couch height for easy patient access, and soft indirect ambient lighting in the gantry opening.

Featuring a 100cm gantry opening, which is larger than those on standard CT machines, Halcyon is capable of rotations 4x faster than c-arm gantries for rapid imaging and treatment. The system is also capable of fast and sharp volumetric imaging in as little as 15 seconds. With Halcyon treatments, a complex image guided IMRT plan is clinically accelerated compared to those delivered on traditional devices.



Operationally, Halcyon features a streamlined workflow that only requires nine steps from the start to the end of treatment compared to up to more than 30 steps with older technologies. To assist in the reduction of time and construction costs from installation to first patient treatment, Halcyon comes pre-commissioned, requires less shielding than traditional systems, can fit in a vault as small as 5.9 meters (19.68 feet) x 5.539 meters (18.17 feet) x 2.743 meters (8.99 feet) high and can be installed in two weeks or less.

For more information on Halcyon visit www.varian.com/halcyon

About Varian

Varian focuses energy on saving lives and is the world's leading manufacturer of medical devices and software for treating and managing cancer. Headquartered in Palo Alto, California, Varian employs approximately 6,500 people around the world. For more information, visit www.varian.com and follow @VarianMedSys on Twitter.

Provecs Medical on Gene Therapy in Oncology

Provecs Medical GmbH is pleased to report in December 2017 that, in the journal Human Gene Therapy, is a comprehensive overview* of gene therapy attacking multiple targets that it has pioneered.

Provecs, a cancer immunotherapy company developing novel treatments to modulate the tumour microenvironment helps in approaches to immuno-oncology attacking multiple targets with a single drug.

"It is known today that a successful strategy against cancer needs to act on multiple targets or pathways of the immune system in parallel to ensure that it recognises and eliminates tumour cells. In past decades, gene therapy research has developed a vast array of technologies not only to transfect all sorts of cells and tissues, ex vivo as well as in vivo, but also to organise, regulate and stabilise the genetic content of the vectors. Gene therapy therefore is the best available toolbox for the targeted delivery of several therapeutic entities to the tumour and its microenvironment. It was our goal to summarise the impact of gene therapy on novel approaches in cancer therapy that may well lead to breakthrough treatments against tumours," said Dr Frank Schnieders, CEO of Provecs Medical.

Provecs is a pioneer in the tumour gene therapy field and has developed ENVIRO, a unique, patented adenoviral platform for the targeted delivery of up to four biologicals combined in one product. The first product candidate, Immunalon®, is expressing three potent immune-modifying signaling proteins - Interleukin-12, Interleukin-2 and CD137 ligand - to turn off tumour-mediated immune suppression and to promote T- cell infiltration of tumours and recognition of cancer cells. These molecules stimulate the activation, proliferation and survival of a synergising network of tumour-defensive immune cells in both the innate and the adaptive immune system. At present, Immunalon® is being developed for the treatment of a wide range of solid cancers. In urinary bladder cancer, it is partnered with Medac Gesellschaft für klinische Spezialpräparate mbH (Wedel, Germany).

provecs medical

Provecs Medical GmbH

Provecs Medical is a private biopharmaceutical company, based in Hamburg (Germany) and specialised in immune-oncology. Based on its multivalent adenoviral ENVIRO technology platform, the company has developed unique solutions to re-program the immunologic barriers in the tumour microenvironment. Provecs has established a comprehensive proof-of-concept platform, named EXVIRO, for ex-vivo therapy simulation in primary human cancer tissues. Immune processes are monitored by big data transcriptome profiling, bioinformatics, and tissue immune imaging technologies. Provecs´ lead product Immunalon® is being developed for the treatment of solid cancers with a focus on urinary bladder cancer. www.provecs.com

Contact: Dr Frank Schnieders, CEO,
E:schnieders@provecs.com
T: +49 (0)40 4 12 63 26 83

**Immuno-Oncology - the Translational Runway for Gene: Therapyhttp://online.liebertpub.com/doi/pdfplus/10.1089/hum.2017.145.*

European Launch of "Call to Action" in Precision Cancer from Queen's University, Belfast

Professor Mark Lawler's (Queen's University, Belfast, N Ireland has launched 'Call to Action' in the European Parliament for the widespread employment of cancer biomarkers to underpin a precision cancer medicine health strategy for European citizens. Speaking in the European Parliament in Brussels, as part of a European Cancer Patient Coalition (ECPC) event hosted by Member of the European Parliament Marlene Mizzi (S&D, Malta), Professor Lawler said, "It is critical that we use biomarkers to enhance our ability to detect cancer at the earliest possible stage and to employ biomarkers to inform our clinical management of patients following treatment. "Without access to clinically relevant biomarkers, it will not be possible for Europe to realise the promise of precision medicine and personalised healthcare, thus disadvantaging European cancer patients from receiving the best possible care for their disease.

"Biomarkers can detect cancer earlier, select best treatment options for patients and spare patients the debilitating side effects of treatments that will have no therapeutic benefit. If used appropriately, they can also lead to cost efficiencies and cost savings within health services across Europe."

Professor Lawler highlighted how research at Queen's University Belfast is at the forefront of this precision medicine revolution and is driving a research-enabled comprehensive cancer care agenda, involving patients, academia, healthcare and industry, which he saw as a model to be scaled-up at European level. Queen's reputation in this area of healthcare is also reflected in the decision of the European Alliance for Personalised Medicine, the premier European policy organisation, to have its inaugural congress in Belfast.

For more information on The European Cancer Patient Coalition (ECPC), visit http://www.ecpc.org
For more information on The European Alliance For Personalised Medicine visit https://www.euapm.eu/
Media Enquiries to Sian Devlin, s.devlin@qub.ac.uk or (+44) 28 9097 5292.

A Niche for Metastases – From the Technical University of Munich (TUM)
– Pancreatic cancer paves the path for metastases in the liver at an exceptionally early stage

Pancreatic cancer is one of the most aggressive forms of cancer, which frequently metastasises to such organs as the liver before the tumour has been detected. The molecular mechanism that underlies this ability is now being unravelled by Professor Achim Krüger's team in TUM [1]. Increasing interest has been taken in TIMP1 because of its anti-protease activity. Proteases have long been considered of relevance in cancer spread because they can open pathways by their enzymatic activity, allowing tumour cells to get into blood vessels and infiltrate other tissues. It follows that TIMP1 could block this activity and act as an anti-cancer treatment.

Paradoxically, however, the research has shown that, in many cancers, increased TIMP1 is associated with a poor prognosis, and actually leads to aggressive spread. Thus TIMP1, according to Krüger's research, has other hitherto unknown functions. TIMP1 is being produced and secreted in the early undetected stages of pancreatic cancer, as also in conditions such as chronic pancreatitis. It gets transported to the liver where it interacts with CD63 found in the stellate cells. These cells are usually inactive but become active in pathological conditions of the liver. The binding of these two molecules leads early on to activation of the stellate cells, which creates niches in this organ to which tumour cells can metastasise and this might be occurring even before this aspect of malignancy has been reached. The work continues on this niche forming process, but the focus now is on trying to prevent this crucial binding to CD63. This is the best way of halting the process because suppressing TIMP1 itself would not be beneficial as its inhibitory action on proteases is needed for many bodily functions, including reducing the possibility of metastatic spread to other tissues than the liver.

Reference
1. Grunwald B et al. *Pancreatic Premalignant Lesions Secrete Tissue Inhibitor of Metalloproteinases-1, Which Activates Hepatic Stellate Cells Via CD63 Signaling to Create a Premetastatic Niche in the Liver.* Gastroenterology. 151(5):1011-1024, 2016 . doi: 10.1053/j.gastro.2016.07.043.

Oasmia Pharmaceutical receives marketing approval for Paclical® in Kazakhstan

Oasmia Pharmaceutical AB (NASDAQ: OASM), a developer of a new generation of drugs within human and veterinary oncology, announced in December 2017 that it has received marketing approval for Paclical in Kazakhstan. Paclical is the first water-soluble cancer drug with paclitaxel to receive a market authorisation. Paclical will be sold through Hetero Group and is planned to be launched during the first half of 2018.

Paclical, called Apealea in Europe, is a novel formulation of paclitaxel based on Oasmia's proprietary XR17 technology. It was approved for treatment of epithelial ovarian cancer. XR17 is non-toxic and forms water-soluble nanoparticles with paclitaxel.

"The relationship established this year with Hetero Group grows further according to our plan with this approval. We are pleased to see this expansion into Kazakhstan, a country that we are confident will benefit from an additional and high-quality treatment now made available to physicians and patients. We look forward to Hetero's work in generating sales in the region, and most importantly to Paclical making a difference in the lives of patients and their families" said Julian Aleksov, Executive Chairman at Oasmia Pharmaceutical.

Oasmia Pharmaceutical AB
Oasmia Pharmaceutical AB develops, manufactures, markets and sells new generations of drugs in the field of human and veterinary oncology. The company's product development aims to create and manufacture novel nanoparticle formulations and drug-delivery systems based on well-established cytostatics which, in comparison with current alternatives, show improved properties, reduced side-effects, and expanded applications. The company's product development is based on its proprietary in-house research and company patents. Oasmia is listed on NASDAQ Capital Markets (OASM.US), Frankfurt Stock Exchange (OMAX.GR, ISIN SE0000722365) and NASDAQ Stockholm (OASM.ST).

For more information: Julian Aleksov, Executive Chairman,m T: +46 18 50 54 40, E: julian.aleksov@oasmia.com

Agendia Inc: AJCC Confirms MammaPrint's Clinical Utility for Treatment Decisions and Staging in Recent 8th Edition Breast, Chapter Update

In Irvine, CA, USA and Amsterdam, the Netherlands (November 20, 2017), Agendia Inc, a world leader in personalised medicine and molecular cancer diagnostics, announced that the American Joint Committee on Cancer (AJCC) has recently issued a Breast Cancer Update and Correction which revised and clarified the Cancer Staging Manual, 8th Edition regarding the use of multigene genomic profiles for Pathological Prognostic Staging [1]. An Expert Panel update clearly states that obtaining a genomic profile is not required for assigning Pathological Prognostic Stage. They do not endorse the use of any specific multigene genomic panel. These statements clarify that the use of MammaPrint is compliant with Commission on Cancer – National Accreditation Program for Breast Centres (CoC-NAPBC) accreditation standards.

One implication of this update is that, unlike MammaPrint, the use of one multigene panel (21-gene assay) will require specific monitoring by breast centres for down-staging a limited and infrequent number of patients. This may require breast centres to implement costly and complex systems. From The New England Journal of Medicine [2] and the latest American Society for Clinical Oncology (ASCO) guideline update [3], the AJCC Task Panel recognises that MammaPrint has Level 1 evidence, based on MINDACT, for determining clinical prognosis. MammaPrint is currently the only risk of recurrence in breast cancer test that is recognised by ASCO and AJCC for use in clinically high risk patients.

Dr William Audeh, Chief Medical Officer at Agendia, said: "Agendia is pleased to see AJCC has clarified that genomic profiling is not necessary for staging, and that the main reason for ordering these tests is to provide clinically relevant information which helps physicians make adjuvant therapy decisions. The recent ASCO Breast Cancer Guideline and now this AJCC update confirm the Level 1 clinical utility evidence for MammaPrint from the MINDACT trial."

Contacts: Instinctif Partners (Agendia), Ashley Tapp / Lynne Trowbridge / Samantha Cheung, T: +44 (0)20 7866 7923, agendia@instinctif.com

1. American Joint Committee on Cancer. M.B.Amin et al. (eds.) AJCC Cancer Staging Manual, 8th Edition-Breast Chapter Update. Nov 10, 2017.
2. Cardoso F. et al. N Engl J Med. 2016 Aug 25;375(8):717-29. DOI: 10.1056/NEJMoa1602253.
3. Krop I, et al. Journal of Clinical Oncology 35, no. 24 (August 2017) 2838-2847. DOI: 10.1200/JCO.2017.74.0472.

From The Institute of Cancer Research, London – European Medicines Agency approves abiraterone combined with hormone therapy as first-line treatment for advanced prostate cancer

The prostate cancer drug, abiraterone, has been approved by the European Medicines Agency in combination with standard hormone therapy for use as a first-line treatment for advanced prostate cancer. Men with newly diagnosed prostate tumours that are 'high risk' with spread already occurring will be eligible for the combination, which delays progression by over a year longer than standard hormone treatment alone. Abiraterone was discovered at The Institute of Cancer Research, London, and had already been approved for the treatment of advanced prostate cancer before chemotherapy in men, for whom hormone therapy had failed.

The new decision has been based on data from an international multicentre phase III LATITUDE trial, which showed that the combination had a clear benefit when used earlier. NICE is currently carrying out an appraisal of abiraterone in this setting, with a decision expected in 2018.

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said: "It is fantastic news that abiraterone has been approved by the European regulator as a first-line treatment in combination with hormone therapy for men newly diagnosed advanced prostate cancer. Drug therapy for prostate cancer has undergone a revolution over the last decade, and this is another big step forward – the first time that a modern, targeted therapy has been approved for use from the point of diagnosis. Abiraterone has already improved the outlook for hundreds of thousands of men with the disease worldwide. Following fantastic results from clinical trial results published earlier in the year, it is clear that using abiraterone right at the start of treatment can be hugely beneficial – delaying cancer progression by over a year compared with standard hormone therapy alone. "We hope that NICE and the manufacturer will work together to ensure that abiraterone is made available at an affordable price, so that the combination with hormone therapy can be approved for use on the NHS as soon as possible."

For more information please contact Claire Hastings in the ICR press office on 020 7153 5380 or claire.hastings@icr.ac.uk. For enquiries out of hours, please call 07595 963 613.

Genoscience Pharma receives FDA approval for Phase Ib/IIa study of GNS561 in liver cancer

Genoscience Pharma (www.genosciencepharma.com), Marseilles, France, December 6, 2017, reports that GNS561 has received approval from the Food and Drug Administration (FDA) to initiate a Phase Ib/IIa study in patients with advanced hepatocarcinoma (HCC).

This is the First-In-Human study to be conducted under the Investigational New Drug (IND) protocol approved by the FDA. The Phase Ib/IIa study will evaluate the safety, activity and pharmacokinetics of escalating doses of GNS561. Up to 36 patients will be enrolled in six cohorts during the dose escalation phase. Additional patients will be enrolled in the continuation phase to obtain a total of 20 evaluable subjects at the recommended dose. "The FDA approval of our first IND application is a major milestone for Genoscience Pharma," said Philippe Halfon, chief executive officer. "This strengthens our position as a drug discovery and development company focused on the development of innovative anti-cancer drugs for the betterment of patients. We believe that GNS561, acting through a novel mechanism of action, has the potential to change the treatment paradigm of HCC. We value our collaboration with the FDA as well as other government authorities that reviewed our submission. We look forward to sharing the details of our upcoming Phase Ib/IIa trial."

About GNS56

GNS561 is a novel Solute Carrier Transporter (SLCT) inhibitor demonstrating potent antitumour activity against a panel of human cancer cell lines, including HCC. GNS561 also shows activity in cell lines resistant to current standard-of-care treatment options for HCC.

GNS561 is an orally bioavailable compound initially being developed for the treatment of primary liver cancer, including advanced HCC. GNS561 is also being investigated pre-clinically in other solid tumours.

The ROYAL MARSDEN
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The Royal Marsden Conference Team

Calendar of Conferences 2018/19

March

15 5th Symposium on Molecular Pathology in Oncology – Hot topics

21 Integrating Inherited Cancer Syndromes into Cancer Care

April

18 A User-Guide to Cancer Immunotherapy

June

21 The Royal Marsden Neuro-Oncology Conference

September

10-11 Gynaecology Conference (Exenteration (2-day) study day)

12 A User-Guide to Cancer Immunotherapy

October

05 The Royal Marsden Testicular and Bladder Cancer Meeting

11 The 10th Annual Conference on 'Anaesthesia for Major Surgery: What's new?

12 The 11th Annual Royal Marsden Breast Cancer Meeting: Hot Topics in Breast Cancer

November

09 The 10th Annual Royal Marsden Head and Neck Conference A Decade of Progress in Head and Neck Cancer Management

15-16 The Royal Marsden Pain and Opioid (2-day) Conference

December

10 Cutting Edge Management of Pancreatic Cancers

17 The Royal Marsden Thyroid Conference

For further information
Email: conferenceteam@rmh.nhs.uk
Tel: 020 7808 2921
Fax: 020 7808 2334
www.royalmarsden.nhs.uk/conferences


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