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A new chapter begins for EORTC

A reorganisation at the EORTC Headquarters should reinforce its position as a leading and independent cancer research organisation, key insiders say. The move coincides with the culmination of efforts to prioritise the clinical research undertaken by the organisation. Both changes are aimed at adapting EORTC to the needs of clinical and translational research in the 21st century.

'The Executive Committee and the Board wish to become more involved with the co-operative groups strategies, to help and support them,' said Dr Françoise Meunier, EORTC's director general. 'I really believe that this way we can give groups more help to conduct the projects in line with global EORTC strategy defined by the Board.

'For example, we created the Early Project Optimization Department as part of the reorganisation; new projects will need a green light from the Executive Committee before going any further. It will mean on one hand that we don't devote time and energy to studies that, in the end, would be rejected anyway by the Protocol Review Committee. Other projects, though, will receive valuable input on their design and concept at this early stage,' she said.

At the EORTC Headquarters, a nominal two branches have been created. Long term EORTC staff member Dr Denis Lacombe has been appointed scientific director; Dr Rémy von Frenckell, who joined the EORTC in September 2007, becomes director of methodology and operations. Both report directly to Dr Meunier.

'We wanted to adapt EORTC's Headquarters structure to meet the needs of pan-European academic research and our partnership with the pharmaceutical industry,' she said.

Dr von Frenckell said he was 'extremely happy' to take over methodology and operations. He spent 15 years as a medical statistician in academia, and became associate professor at the University of Liège. He moved from there to the pharmaceutical industry, working for Bristol-Myers Squibb, and then UCB, a Belgian pharmaceutical company.

He stressed that EORTC Headquarters has not been divided into 2 separate parts: 'EORTC remains a matrix organisation whose success will be directly linked to collaborations across both branches. The new structure is designed to perform and to strengthen our current position. The two sides will each reinforce the other, the better the methodology and the operations, the easier it will be to accomplish our goals.'

Dr von Frenckell said the reorganisation of the Headquarters would help EORTC fulfil its mission to improve the standard of cancer treatment through close collaboration with NCI and many national and international research groups. 'First of all, EORTC has to be positioned as an academic research organisation (ARO) as opposed to a contract research organisation (CRO).

'Our independence, the control over design of the study and key parameters of the data bases, and the interim and final analyses as well as right to publish are key words of our mission.

Left to right: Dr Denis Lacombe, Scientific Director, Dr Françosie Meunier, Director-General, Dr Rémy von Frenckell, Director of Methodology and Operations.

'We want to increase recognition of academic research organisations like EORTC. I am more and more convinced that these independent groups will

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EORTC Reorganisation continued...

be looked at by health authorities as adding value in a very near future.'

His years in the pharmaceutical industry would help him in future negotiations, he said. 'Pharmaceutical sponsors are very demanding, and of course, some of what they ask for is mandatory. But it is important to be able to discuss and come to mutual understanding. I want to make sure that the work we do is related to our mission and has scientific value.'

Dr Denis Lacombe has worked at the EORTC since joining on a fellowship programme 14 years ago. He is a clinical research physician and has worked, variously, on protocol development, the appropriate conduct of studies, safety reporting, final analyses, phase I, II and III trials in brain, head and neck tumours. He set up departments in pharmacovigilance and regulatory affairs and was responsible for Intergroup Office, which ensures appropriate interactions with sister organisations within and outside Europe.

'My responsibility now is mainly to ensure that across EORTC, the scientific strategy defined by the Board is facilitated.'

'Some of our networks are very mature and active and know where they are going. But some face problems if, for example, they want to run a trial on a new agent, and the company is not keen to collaborate because the tumour type does not represent a big market. We will help find a solution.

'We want to progress in a logical manner and promote 'clinicogenomic' trials with relevant translational research. If we do a clinical trial we know why we are doing it, that it addresses a question which arose in a previous trial, and that it will bring new knowledge. A clinical trial is not a 2-3 year activity; it has to be integrated into a development and strategical plan of a group of investigators collaborating on the same disease for many years with a coherent approach to establish state of the art treatment and to change practice.

'Indeed, the EORTC wishes to participate in the development of new more effective or less toxic treatments but also in establishing optimal therapeutic strategies based on multidisciplinary work outside the context of drug registration.

'We will look at clinical research in a different way. Now, trials will also be biology-driven, or have a serious biology component, so that they address mechanistic questions, assess specific signatures or identify predictive markers. We want to improve our understanding of what an agent or combination does in a certain population.

'Clinical research has dramatically changed and we have to adapt to this environment. Ideally we want to run large clinical phase III trials with a translational component which addresses a key biological question that will change the treatment of patients.

'But we remain active in earlier stages of development because that's

continued over

Agreements reached with cancer centres

The internal reorganisation completes a process of change at EORTC which has been ongoing for the past 3 years. The decision was made to prioritise truly innovative clinical research, so that the EORTC took on only trials likely to change clinical practice, preferably those involving interaction between different disciplines, and those with a strong translational component.

An extensive series of meetings with the chairs of all cooperative groups has been carried out by the EORTC President, Dr Martine Piccart (Institut Jules Bordet, Brussels, Belgium) and the Executive Committee.

New biology-driven trials involve close cooperation between laboratory scientists and clinicians, and the EORTC will in future promote very complex trials within a network of cancer centres, known as NOCI (Network Of Core Institutions).

The centres involved were always big recruiters of patients into trials, but also have special competence in fields such as genomics, proteomics or molecular imaging.

The institutions will be linked by a consortium agreement which state the rules, for example, those pertaining to intellectual property rights. Dr. Piccart said, 'The contracts define who owns the rights if someone at a centre makes a discovery during an EORTC trial. The rights will be shared according to the terms of the contract: the inventor and the centre need to be rewarded, but the EORTC was behind the trial, so something has to go back to the EORTC.'

Linking institutions with this upfront agreement should help streamline the bureaucracy which often

EORTC President, Dr Martine Piccart

holds up trials; it can take 3 years for a trial to start. Dr Piccart: 'The MINDACT trial embodies translational research, it is led by EORTC which coordinated and planned it, and it took more than 2 years of negotiation with lawyers to reach agreement with everyone involved. You can't do that with every protocol in the pipeline. The experience convinced us that we need to put a structure in place, otherwise brilliant ideas get lost. With a pre-existing structure, a good idea can be moved along quickly.'

Dr Piccart said that the agreements with the cancer centres are not in competition with the pre-existing large network of groups. 'This important change is not going to stop the work of the disease-oriented groups which is still crucially important. Findings from clinicogenomic trials will need validation in large studies; we still need the important disease-oriented groups. This change will add value to their work.'

Dr Piccart said she hoped that contracts with 8 important cancer centres would be signed early in 2008, to be joined later by a further 12 centres.

Young Scientists Investigate Pain

Five young European scientists have received grants to support innovative, exploratory research into clinical pain. The grants, totalling Euro 100,000, were awarded by the European Federation of Chapters of the International Association for the Study of Pain (EFIC) and the pharmaceutical company Grunenthal.

The grants are intended for young investigators just beginning their research career and focus on novel ideas in the understanding and treatment of pain. Projects include a study of the attentional processes that modulate pain in the human brain, combining behavioural and neurophysiological methods. The results could help develop psychotherapeutic techniques to help patients cope better with pain. Another study will examine factors which could explain why some subjects – and not others – are predisposed to develop referred pain.

Left to right: Dieuwke Veldhuijzen PhD (University of Utrecht, the Netherlands), Thomas Graven-Nielsen PhD (Aalborg University, Denmark), Markus Ploner MD (Technical University Munich, Germany), Christian Netzer MD (Cologne University, Germany), Valéry Legrain PhD (Université Catholique de Louvain, Brussels, Belgium)

EFIC President and Director, Professor Serdar Erdine (Istanbul University, Turkey) said, 'EFIC and Grunenthal are now in the fourth year of the fruitful tradition of encouraging young European pain scientists in their ambitious work to help understand chronic pain and to provide relief to patients suffering from chronic pain. Both are highly committed to bringing to public awareness the realisation that pain is a disease in its own right.'

New Communications Manager at EORTC

New communications manager, Dr Colette Lukan, becomes the point of contact for communications within the organisation and outside, with industry, policymakers and the public.

Dr Colette Lukan

Dr Lukan is a Canadian radiation oncologist, trained at the University of Ottawa. She worked for 15 years in drug regulation covering oncology and haematology for Health Canada. She has been a consultant radiation oncologist (Grand River Regional Cancer Centre, Kitchener, Ontario, Canada) and has also worked for Hoffman-La Roche, Basel, Switzerland.

She said she wants to expand the lines of communication inside the organisation in order to further EORTC's mission, to educate others about its role and to inform the public. 'I'm an oncologist, I understand the process of clinical trials and science. I can be the point of communication that draws everyone together so that we can move forward.'

EORTC Reorganisation continued...

where the phase III trial is designed. This is much more difficult with new agents because more effort is needed to understand what the drug does before the phase III trial starts. EORTC has a lot of experts with broad knowledge and they bring added value to earlier stage development to ensure that we bring the right phase III trials into existence.

One of the benefits of the reorganisation is that companies will have a central point of contact within the EORTC, Dr Lacombe said, which will ensure that a company working with, say, the brain group and the breast group will receive a single message. 'We are offering professional and comprehensive services to industry, while also defending our principles of independence. We have to enforce the right methodology and analysis.'

Aromatase expression in lung cancer

Aromatase expression might be a useful predictive biomarker for non-small-cell lung cancer (NSCLC) survival (*Cancer Res 2007;67:10484–89*).

Lee Goodglick (University of California, Los Angeles, CA, USA) and colleagues assessed the level of aromatase expression in tumours from 422 patients with NSCLC using a high-density tissue microarray. The findings were confirmed and validated in an independent patient cohort (*n*=337).

Patients with NSCLC who had low expression of the enzyme were predicted to have greater survival than those with high expression (p=0.005). Moreover, this predictive ability was sex and stage specific with low aromatase expression predicting greater survival probability for women with stage I–II disease (p=0.010) than for men (p=0.152).

'Lower levels of aromatase predict a higher probability of survival in a subset [of] women with NSCLC at early stage I–II who [were] 65 years of age and older. By contrast, women with high aromatase expression had a worse prognosis', explains Goodglick.

In addition to allowing a predictive stratification of NSCLC patients, these findings might also suggest novel treatment approaches for NSCLC using currently available aromatase inhibitors, already approved for breast-cancer treatment.

'The finding that aromatase is a marker in early stages of lung cancer is important for our understanding of new pathways in the pathogenesis of lung cancer in women and specifically in non-smoking women', says Karen Reckamp (City of Hope Institution, Duarte, CA, USA). However, an additional study should be run in a prospective manner with a larger cohort of patients to confirm these findings.

Aromatase is part of the oestrogen synthesis pathway, which is crucial in the progression of tumours with oestrogen receptors. Aromatase might play a part in normal lung function as well as in the development of NSCLC.

Marta Paterlini

*This story originally appeared in Lancet Oncol 2007;**8**:1060*

Missing protein 'could improve selection for paclitaxel'

Loss of a protein called TGFBI may cause paclitaxel to fail in the treatment of ovarian cancer, say researchers at Cambridge University, UK. The protein could be used as a biomarker for selecting patients likely to respond to this class of drug.

The researchers (REF), funded by Cancer Research UK and the Medical Research Council, examined ovarian cancer cell lines and data from 20 patients in a prospective trial. Those who had showed no response to the drug had less TGFBI in pre-treatment samples than those who responded. Death of cancer cells appeared to occur where levels of TGFBI were high.

First author Dr Ahmed Ashour Ahmed said that proteins such as TGFBI surround cancer cells and send messages which sensitise them to paclitaxel: 'Deciphering the code by which these messages are sent will enable the discovery of new treatments that will simulate the coded messages, leading to a significant improvement in paclitaxel response.'

The findings could also lead to improvements in the success rate of other taxane drugs in lung and breast cancer.

Positive news in colorectal cancer...

The European Committee for Medicinal Products for Human Use (CHMP) has given a positive recommendation for label extensions for the anti-angiogenic agent bevacizumab (Avastin) and oral chemotherapy capecitabine (Xeloda). The recommendation covers the treatment of advanced colorectal cancer.

CHMP recommends that capecitabine's label should be broadened to include use in combination with other chemotherapies; and bevacizumab's to include its use alongside capecitabine plus oxaliplatin; or with FOLFOX-4 (5-FU/LV plus oxaliplatin). The current label for bevacizumab allows use in combination with 5-FU/LV and 5-FU/LV/irinotecan.

The recommendations are based on 3 phase III trials in which, according to manufacturer Roche, no new safety findings related to either bevacizumab or capecitabine were observed. The company's filing's in Europe followed the submission of a supplemental new drug application (sDNA) to the US Food and Drug Administration (FDA) in March 2007 for the use of XELOX (capecitabine plus oxaliplatin) with or without bevacizumab in the treatment of advanced colorectal cancer.

... and in advanced breast cancer

Lapatinib (Tyverb) has received a positive opinion recommending conditional marketing authorisation from the European Medicines Agency (EMEA), according to GlaxoSmithKline (GSK). Conditional approval would allow use of lapatinib in combination with capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumours overexpress ErbB2 (HER2).

The ruling would apply to patients with progressive disease following prior therapy including anthracyclines, taxanes and therapy with trastuzumab in the metastatic setting.

Lapatinib is an oral therapy which inhibits both ErbB1 (EGFR) and HER2. It is being evaluated both alone and in combination with other therapies across the spectrum of HER2-positive breast cancer.

A conditional marketing authorisation is granted to a medicinal product that fulfils an unmet medical need when the benefit to public health of immediate availability outweighs the risk inherent in the fact that additional data are still required. In the case of lapatinib, GSK is to provide further data from a phase III trial comparing the combination of lapatinib and capecitabine, with capecitabine alone. Existing data suggests that lapatinib may decrease the incidence of relapse in the central nervous system and another study will be conducted to explore this.

PODIUM

Introducing radiotherapy to Oman

Dr Bidhu Kalyan Mohanti is Professor of Radiation Oncology at the All India Institute of Medical Sciences (AIIMS), New Delhi, India. He worked in Oman between 2004 and 2006 where he was involved in establishing the National Oncology Centre at the Royal Hospital, Muscat. Dr Mohanti audited initial use of the country's first radiotherapy department.

How was the experience?
It was enriching and gratifying. Once the building was completed, the entire process of setting up the centre and radiation therapy department was completed in 6 months. The Oman administration is highly professional, responsive and committed to the delivery of quality health care to its citizens. The centre offers radiation oncology, medical oncology, paediatric oncology, radio-diagnosis, nuclear medicine, brachytherapy, a laboratory, pharmacy and medical records. It has attached day-care and in-patient wards, and access to surgery, pathology, and other clinical and para-clinical disciplines.

What facilities existed in Oman at the time the centre was conceived?
Tertiary health care in Oman has developed well since the 1980s, but there was no cancer centre before 2004. Cancer patients in Oman were treated with chemotherapy at the Royal Hospital or University in Muscat, or with surgery at tertiary or regional hospitals. There was no provision for radiotherapy in the country.

What happened to patients who needed radiotherapy?
Every year, approximately 250 patients were referred to other countries at the government's expense. The total incidence of newly diagnosed cancer was 800-1000 cases per year. Assuming half – between 400–500 patients per year – needed radiotherapy, this means that many patients who could have benefited were not receiving treatment. Some felt unable to travel; physicians were also reluctant to send patients with multiple medical problems. Further, even when patients did travel, they could not obtain correctly sequenced multi-modality cancer therapy.

When the centre opened, how many of the patients needing treatment received it?
In the first 6 months, 359 patients were referred for evaluation for radiation oncology, and 287 (80%) turned up for this consultation. Of the consulted patients, 218 (76%) were suitable for radiation therapy, and given an appointment for a course. Overall, 139 patients (64% of those consulted) were treated during the 6 month audit period.

Why didn't patients receive treatment?
For specialised tertiary care such as radiotherapy, patients are referred from the community primary centre to a regional hospital and subsequently diagnosed or suspected cancer patients are referred to the cancer centre. Oman is a large country, with a coast line of 1700 kms, and it is divided into 10 health regions. Patients often have to travel long distances and stay away from their families for the duration of the radiotherapy course. The government provides the treatment free of charge; the community or regional hospital makes transport arrangements for patients and their families; the cancer centre has facilities for patients and families from outside the region to stay. Even so, some patients find it difficult and do not comply with advice to have radiotherapy. There is some fear and lack of awareness about the practice of radiation therapy. One glioma patient's son asked, 'Will it cause an electric shock inside my father's head?'

How can compliance be improved?
Patient compliance is largely a balance between physician advise, patient autonomy and access to information. Patients who are prescribed radiation therapy either alone or combined with surgery/chemotherapy should be appraised about the outcome if radiotherapy is not given, the duration of stay for radiotherapy course and how to organise family affairs. This is done routinely by the specialty doctor/nurse at the clinic, yet greater emphasis is needed. Any fear or reluctance should be addressed by a trained nurse or counsellor. The physician and nurse at community/regional hospital level should follow-up patients who are referred to the cancer centre. Non-governmental organisations and voluntary services could be helpful.

Has the situation has improved?
Doctors and nurses from different regions in Oman have attended training courses on radiotherapy practice and policies. Medical specialties other than cancer are starting to refer patients. Further, more than 90% patients who start a planned prescribed radiation therapy course do complete it.

What are the implications of this work for radiotherapy in the region?
Radiation therapy facilities in most countries of Middle East Asia, Africa are sparse. Since radiotherapy is a cost-intensive health care investment, the proper utilization of the facility is an indicator of the success of cancer care services. Improving physician awareness, information sharing with patient and family carers, and follow-up mechanisms for patient compliance are the key to improving access to radiation therapy in most developing countries.