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NEWS...NEWS...NEWS

Patient forums 'drive policy'

Patient-driven initiatives are becoming an important force in health policy and service delivery, according to speakers at the 4th World Conference for Cancer Organisations (Dublin, Ireland, 17–19, November 2004). They are improving quality of care, breaking down social stigma associated with cancer, highlighting social and economic issues and revealing cultural differences that may need to be actively addressed. They also help keep cancer in the public spotlight, reinforcing the priority accorded to cancer control strategies.

Isabel Mortara, Executive Director of UICC, said, ''Through empowering people with cancer and cancer survivors to voice their opinions, we are seeing a growing body of people who are helping drive real change in the way health services are delivered''.

''Our next goal should be to promote the establishment of patient-driven initiatives in middle-and low-income countries, where patients, particularly women, are beginning to demand a stronger voice in policy and treatment''.

US approval for erlotinib

Erlotinib (Tarceva), an EGFR-targeted treatment, has been approved by the US's Food and Drug Administration (FDA) for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC), after failure of at least one prior chemotherapy regimen.

Erlotinib has been shown to improve survival among patients with NSCLC by 42% (*Proc Am Soc Clin Onc* 2004, Abstract # 7022). The length of time before symptoms deteriorated was increased. Survival at one year was increased by 45%.

The drug is currently under review for marketing authorisation with the European and other health authorities.

HPV vaccine 'shows great promise'

A vaccine against high-risk strains of human papillomavirus (HPV) was 'highly efficacious' in preventing incident and persistent cervical infections, researchers say. The bivalent HPV-16/18 virus-like particle vaccine also prevented associated cytological abnormalities (*Lancet* 2004;**364**:1757–65).

The US/Brazil-based study included 1113 women aged between 15 and 25. They were randomised to receive either 3 doses of the vaccine with adjuvant, or placebo. Women were assessed for HPV infection by cervical cytology for up to 27 months.

Those who were fully vaccinated had 100% protection against persistent infection and 92% against incident infection. This compares with 95% protection against persistent infection and 93% against incident infection among those who did not fully comply with the protocol (intention-to-treat analysis).

The researchers say the data provide ''compelling evidence'' that this vaccine is highly efficacious against persistent HPV-16/18 cervical infection, cytological abnormalities associated with HPV-16/18 and histological development of HPV-16/18-associated cervical intraepithelial neoplasia (CIN). However, the study was not powered to estimate efficacy for histopathologically confirmed cervical lesions.

'WE NEED TO CONFIRM THAT VACCINATION PREVENTS CERVICAL CANCER'

''Our findings indicate that the vaccine could contribute substantially to reducing world-wide rates of cervical cancer. However, large-scale trials with long-term follow-up are needed to extend our findings and confirm that vaccination prevents cervical cancer,'' they write.

The work has important implications for prevention of cervical cancer in countries where screening is limited, they say, and has the potential to reduce the need for additional cytology or colposcopy where screening programmes exist.

In an associated editorial (*Lancet* 2004;**364**:1731–2), Drs. Matti Lehtinen and Jorma Paavonen (University of Helsinki, Finland), note that these HPV strains are associated with chronic infections and diseases, and neoplasms, in many other sites, including vulva, vagina, anus, penis and oropharynx. Preventive vaccination may be as effective against the non-cervical HPV-associated neoplasms, they say.

Long-term passive follow-up of cohorts of vaccinees and non-vaccinees by population-based cancer registries is needed to prove that vaccination ultimately protects against invasive cervical cancer, they say. Questions remain, such as whether use of the vaccine will prompt a resurgence of other HPV types; and when boosters may be required.

However, they believe the remaining questions can be answered and conclude, ''Preventive vaccination against the oncogenic HPV types will soon be available''.

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UK implements embryo screening for cancer

The UK Human Fertilisation and Embryology Authority (HFEA) has been criticised for allowing, for the first time in the UK, genetic screening of embryos for a disease that will not affect I he child at the time of birth.

HEFA granted the license on Nov 1, 2004, to the Assisted Reproduction Unit of University College Hospital, London, UK, to screen for familial adenomatous polyposis Paul Serhal who was awarded the new licence, is also seeking permission to test embryos for *BRCA1* and *BRCA2* genes, as well as for retinoblastoma.

''If the technology is available to get rid of mutated genes that will lead to cancer, it's going to be only a matter of time before tests are offered to patients to eliminate them'', says Serhal. ''I don't see any problem at all with all this. Second on the list is retinoblastoma, and *BRCA1* and *[BRCA2]* will certainly be screened for as well.''

HFEA consulted experts on pre-implantation genetic diagnosis (PGD) for various diseases, including cancers, in 2001. By law, HFEA is allowed to grant licenses based on a decision made by a committee of five people.

Joyce Harper (Centre for Pre-implantation Genetic Diagnosis, University College, London, UK), notes that PGD for *BRCA1* and *BRCA2* is offered in other European countries, and ''they have been amazed that the UK are making so much of these issues''.

Josep Egozcue, an embryo researcher at the Autonomous University of Barcelona, Spain, says that even for disorders where prenatal diagnosis may not be offered, such as *BRCA1* and *BRCA2,* ''if the family has been so affected by a disease that they wish to have a child free from this inherited disorder, then it is right to do this''.

Some experts have criticised HFEA's move. Stuart Lavery (Department of Reproductive Medicine, Hammersmith Hospital, London, UK, where PGD for familial adenomatous polyposis was first done nearly 8 years ago), says: ''there are concerns that instead of regulatory bodies leading to public reassurance, the [HFEA] role may actually be to heighten public anxiety leading to a perceived public genophobia''.

Xavier Bosch

*This story originally appeared in Lancet Oncol 2004;**5**:704*

NICE guidelines for head and neck cancers

The UK's National Institute for Clinical Excellence (NICE) has issued guidance for the National Health Service in England and Wales on how healthcare services should be provided for adults with head and neck cancers. The guidance is intended for those who develop and deliver cancer services.

The document recommends that assessment and treatment services should become increasingly concentrated in cancer centres serving populations of more than one million people. It stresses the need for multidisciplinary teams, but says specialised teams will deal with patients with thyroid cancer and with those with rare or particularly challenging conditions such as salivary gland and skull base tumours.

Arrangements for referrals should be streamlined and diagnostic clinics should be established for patients with neck lumps. A wide range of support services should be provided, including clinical nurse specialists, speech and language therapists, dietitians and restorative dentists.

Professor Peter Littlejohns, Clinical Director at NICE said, 'For health services, head and neck cancers present particular challenges because of the complexity of the anatomical structures and functions affected, the variety of professional disciplines involved in caring for patients and the relatively sparse geographical distribution of patients requiring specialised forms of therapy or support. This guidance… clearly sets out the services that should be available'.

'Improving Outcomes in Head and Neck Cancers (cancer service guidance) can be found on the NICE website at www.nice.org.uk

Promising early results with VEGF inhibitor

An inhibitor of vascular endothelial growth factor (VEGF) shows activity in pre-treated phase I patients who failed on conventional treatments, US researchers report. ''This is very exciting and may herald a new pattern of clinical practice'' said Dr. David Quinn (University of Southern California, Los Angeles, USA).

VEGF is a critical factor in the development of new blood structures – angiogenesis – which is essential for a tumour to grow. Elevated levels of VEGF often predict poor survival in cancer patients. The inhibitor (VEGF-AS, Veglin) is an anti-sense molecule that targets 3 types of VEGF (A, C and D). It produces a mirror image of the gene that then blocks its activity (*Annals of Oncology* 2004;**15** (suppl. 3), Abstract # 377).

Veglin was given intravenously to 47 patients over 5 days for one or more courses. Toxicity was minimal and the maximum tolerated dose was 200 mg/m^2. Responses were seen in a variety of diseases including T-cell Non-Hodgkin's Lymphoma, renal cell carcinoma and Kaposi's Sarcoma. The drug costs US$ 400/month.

Speaking at the 29th ESMO conference (Vienna, Austria, 29th October–2nd November, 2004), Dr. Quinn said VEGF-A levels were suppressed in most patients, providing a surrogate marker of activity that can be easily sampled. But some patients showed a rise in VEGF-A, which could be due to differences in downstream effectors and mechanisms of resistance. Further studies in renal cancer are planned, using Veglin alone or in combination. Animal models suggest that an oral application may be possible, he said.

Dr. Elizabeth Eisenhauer (National Cancer Institute, Canada) said ''This is another VEGF inhibitor with early evidence of safety. The impact of this and other inhibitors awaits more clinical testing''.

Emma Cannell

Vienna

Tobacco treaty comes into effect

The Framework Convention on Tobacco Control (FCTC) comes into effect early in 2005, following its ratification by 40 nations. Peru, the 40th nation, ratified the FCTC on 30th November, 2004, triggering a provision to implement the treaty in 90 days.

UICC Strategic Leader for Tobacco Control, Dr. Yussuf Saloojee, said, ''The FCTC is off to a strong start but great challenges remain. We are still at the beginning of the process. To fully implement the FCTC will require a global commitment and years of hard work''.

The FCTC is a comprehensive tobacco control agenda including elimination of advertising and promotion (except where nations' constitutions prohibit a complete ban) warning labels on front and back of every pack, prohibition of descriptors such as 'mild', protection from passive smoking, and strict regulation of tobacco product contents. It calls for higher tobacco taxes, global co-ordination to fight tobacco smuggling and promotion of tobacco prevention, cessation and research programs.

Of the 168 countries that signed the treaty, 128 have yet to formally ratify it. However, Dr. Salojee predicts that the pace of ratification will pick up as the treaty comes into force. ''Most countries don't want to be left out'', he said.

Tobacco use killed an estimated 100 million people in the 20th Century and current trends suggest that one billion people may die because if it this century. The UICC says the burden of disease and death is shifting rapidly to low-income countries as most high-income countries are implementing effective tobacco control policies.

Smoking banned in Scotland…

The Scottish government has announced plans for a comprehensive ban on smoking in enclosed public spaces. Legislation was expected to be introduced to Parliament by the end of 2004, and to be in place by the spring of 2006.

Announcing the move, First Minister Jack McConnell said, ''I believe that there is no greater action we can take to improve the well-being of children and families in Scotland, for generations to come, than to secure this legislation and make Scotland's public places smoke-free''.

Licensees or employers who fail to enforce the law will face fines up to a maximum of 2500. Licensees who persistently refuse to comply risk losing their liquor licence.

The ban was widely welcomed by health campaigners and cancer charities. Professor Alex Markham, Chief Executive of Cancer Research UK, sent a message of congratulations. ''Huge numbers of lives will be saved as a result of this legislation and many smokers, desperate for the support to give up, will have a golden opportunity to quit successfully''.

The Scottish Licensed Trade Association has objected to the ban and warned of job losses. But deputy First Minister Jim Wallace said the case for a ban ''is now incontestable, the support overwhelming. It will have worldwide appeal. Potentially there is an opportunity for Scottish business. They should seize that chance. I am in no doubt at all that this move is in the best long term interests of Scotland's health and economic well-being''.

The ban in Scotland follows similar moves in Ireland and in New York. Jack McConnell said that, following these bans, cigarette sales have dropped by 13% in New York and by 16% in Ireland. Professor Markham said that, in Ireland, 7000 smokers stopped within 6 months of the new law coming into effect.

…but England lags behind

Meanwhile, the White Paper on Public Health for England stopped short of a comprehensive ban. Smoking is to be banned in the workplace, restaurants and in pubs that serve food. However, smoking will continue to be allowed in the estimated one in five pubs which do not serve food.

Health campaigners recognised that progress had been made, but were disappointed that the Health Minister, John Reid, had stopped short of a total ban of smoking in enclosed public places. Mr. James Johnson, Chairman of the British Medical Association, said, ''What concerns me is that by not introducing a complete ban, some pubs may find loopholes in the law to allow smoking. For example, if landlords brought in pre-prepared sandwiches, would smoking be permitted?''

Professor Markham said, ''It seems bizarre that the Government has accepted the wisdom of a ban but is then happy to deny the benefits of it to people who work in private clubs and pubs where food is not served. It's like having the legislation to fit all cars with seatbelts because we know seatbelts save lives, and then stopping some passengers from wearing them''.

Mr. Johnson also questioned the timescale, as the English measures are not due to be implemented until 2008. ''When lives need saving, doctors act immediately. John Reid should follow this lead''.

The White Paper commits the UK Government to review nicotine regulation. Professor John Britton, chair of the Royal College of Physicians (RCP) Tobacco Advisory Group welcomed this move and said, ''We… will fully support initiatives in this area to make safe forms of nicotine available to smokers''.

The Paper, 'Choosing Health', also introduced measures to promote healthier eating and increase physical activity. Partnerships between the food industry, advertisers and the government were suggested. But Professor Peter Kopelman, Chair of the RCP's Nutrition Committee said there was no clear timetable for the initiative. ''There has already been a significant amount of consultation over these issues – what we need now is action''.

PODIUM

EORTC: Back on Track

Alexander Eggermont (Professor of Surgical Oncology, Erasmus University, Rotterdam, The Netherlands) specialises in the treatment of melanoma and soft tissue sarcoma, and developed limb salvage programs in Europe based on TNF-isolated limb perfusion. He is President of the EORTC (2003–2006) and has faced the task of rebuilding the organisation after recent problems.

Professor Alexander Eggermont

What went wrong at EORTC?

A number of problems surfaced in 2002/2003 of which the financial problems were the most pressing. In the 7 previous years, we had a budget surplus and were increasing the number of teams and of staff at the Data Center. In 2002, that suddenly went into reverse and we faced a deficit. Several contracts with pharmaceutical companies were delayed which was a reflection of the general slow down of the economy and the first signs that the pharmaceutical industry was suffering. The introduction of the EU Directive on Clinical Trials increased the regulatory complexity and costs of academic non-sponsored trials, which represents 2/3 of our activities, and also made industry more hesitant, from 2003, to start trials in Europe. All of this had a huge impact on an organisation like ours.

How were EORTC's problems addressed?

Structural reforms have been ongoing since September 2003. We very rapidly decreased the staff at the Data Center substantially, from 138 to 100, which we considered the minimum to function. It was an enormous percentage decrease, but fortunately the vast majority of staff departures came from not renewing temporary contracts. There was an enormous amount of work reallocation among staff but it meant that we could continue.

The organisation has become much more flexible. Data Center staff now handle more than one type of job and work for more than one team. Their workload has been increased and may be more burdensome but it may also be more interesting and diverse than before. Understanding the differences between groups may allow us to apply the best of each group elsewhere. When times are difficult, everyone becomes more critical. It's a cycle that all organisations go through, not just EORTC.

It must have been a stressful time for all concerned?

It was. The staff at EORTC Headquarters/Data Center really showed tremendous character, dedication and resilience over this period. But it became clear by mid 2004 that the budget for that year was under control. At present, a conservative estimate suggests we will be in surplus for 2004. A number of very positive developments have allowed us to build up a contingency fund for Data Center staff salaries, so that we will not face an emergency situation again.

What were the positive developments?

We were fortunate in that we had undertaken a study on an educational grant adding temozolomide to radiotherapy after resection of glioblastoma. The study had a positive outcome and we were reimbursed later for work we had already carried out at the level needed for registration. It meant we could reimburse the participating groups and investigators for costs incurred during the trial, and also have a substantial amount left over to build up the contingency fund. Some important new legacies also came in; and we were able to re-allocate existing legacies to stabilise the organisation.

How big is the contingency fund?

During 2004, it went from zero to 5 million. We need 7 million for a year's salary for the Data Center staff, and we're now sure to reach that in the early part of 2005.

What other steps did you take?

We decided to create an academic trial research fund to ensure that EORTC can still carry out its primary function. Academic trials, rather than registration trials, still define the majority of standard treatments in oncology, typically by testing an ''old'' drug for new indications or in combination with another drug or with radiotherapy. There is an enormous need for this work, and if we don't do it, nobody will, but it is totally under-funded.

How much difference has the Clinical Trials Directive made?

The costs of academic trials have increased 3-fold because of the increased demands in management of regulatory affairs, protocol approval, national level committees, increased reporting, data management and so on. We have traditionally funded academic trials out of the surplus from contracts with Pharma. Investigators have often accepted lower fees to save money for the organisation and allow us to conduct academic trials. But over the years, registration trials have become so incredibly labour intensive and expensive that the margins left over for academic studies have been squeezed. The situation is precarious.

Our researchers have plenty of ideas, they are asking questions and want to study them. But the finances for this work are not available due to uncontrolled rising costs.

Why is it so difficult to raise funds in Europe?

Continental Europe does not have the strong charity culture of the US. The prevailing attitude is that our high taxes should cover medical trials. And we have failed to do anything positive about our image. We need to organise patient platforms which are far more interesting to politicians than medical researchers.

We still have some way to go, but we can't do everything at once. First we had to make sure our organisation was sound. But now we have taken on a new public relations professional and will be communicating to patients, the media and politicians about our work and our unique organisation. No other cancer organisation in the world devoted to clinical trials involves so many nationalities and cultures. It is an extraordinary environment of scientific and cultural exchange – and exists without central EU-funding. For its cultural success alone, EORTC deserves substantial EU-subsidies!

How far will EORTC's academic trial research fund help?

It will enable us to set up new academic trials from the second half of 2005. However, all trials will have to go through a competitive process to select trials of the greatest importance and of excellence. This means sophisticated trials with important mechanistic and translational research components. They will be costly, but will yield important results and provide milestone answers. It means EORTC will not launch more than one or two such trials per year, and it will take a substantial research fund to give the green light to the first trial.

There is no going back to the mid 1990s, when research was cheaper and we were able to conduct a greater number of trials. Now we have to be much more selective and it is not an easy message. It will take a cultural change inside the organisation to adjust to the new situation. We will do fewer trials, and only excellent trials. We have to implement this policy, we have no choice.

Our portfolio included some trials that will not necessarily change the standard of care; or trials which have been outpaced by other developments and are no longer essential. We're now continuously critically appraising trials.

Has the structure of EORTC changed irrevocably?

When there is more money around, we will be able to grow again, but we want to remain lean. It usually takes financial pressure to discover how lean you can be.

The general assembly will include representatives of 15 major cancer centres for the first time. Moreover we will create a Network of Core Institutions, comprised of the major cancer centres/academic institutions that comprise the hard core of the EORTC both in accruing power and infrastructure to do the translational research that these days is a mandatory component of meaningful clinical research. Many trials address fundamental questions in genomics, proteomics, pharmacokinetics, advanced pathological examinations.

If you don't focus, select and bring benefits to the core of your organization you will surely (and justly) die. The wake up call will go through the whole organization and will be understood. We have become a more modern and open, democratic organisation. We didn't intend to be closed before, but basic aspects of our structure hadn't changed in 15 years. It was time.

Could the same thing happen again?

We have been criticised for the time it took us to discover the magnitude of the problem. But it was not illogical, because we had previously had such a long trouble-free period. When the world changed with fall-out at both the pharmaceutical regulatory affairs level and the EU Directive, it took some time to identify the problems caused to our organisation: its structure, fabric and workload. EORTC was not different to other multinational institutions in its reaction.

We are now much more streamlined, have financial protocols in place, and are much more critical about our functions.

Will EORTC continue its political activity?

EORTC has been extremely active in communicating to the European Commission the myriad of negative effects from the EU Directive for academic clinical research, especially in oncology. Oncology is different from other fields of medicine in that drugs approved for one indication are often used elsewhere. So drug development is different from that in cardiovascular or infectious disease, and it suffers more from the EU Directive.

We have been successful in adapting Belgian law to limit the damage of the Directive, and this has served as a model for the law in France, Germany and Holland. In fact, politicians in Brussels and Strasbourg have received so many negative messages about the Directive that they recently initiated the process to adapt the law for academic research. It is likely to take a couple of years before implementation, but we had a meeting in Brussels in November 2004 and I'm optimistic that we can repair the damage more quickly than we believed only a few months ago.

What is happening now at EORTC?

We will have a hard core of major academic institutions; an outer core of large peripheral centres and an outer shell of many small hospitals which accrue patients but don't provide the research infrastructure. Young academic researchers tend to work in the institutions in the inner 1–2 layers and we need to draw them into our organisation if we are to survive. The best way to engage young oncologists of any discipline is to directly involve them in translational research projects; which may help them with their PhD thesis, with the curriculum, generate professional interest and be beneficial to them. If we don't, we will miss out on attracting the next generation to our organisation. We intend to allocate research projects involving data management, site visits and regulatory affairs to the institutes, in order to involve young professionals. Many of us are grateful to the EORTC because of how it has shaped our professional careers. EORTC is a career opportunity for young people and our future depends on the message that taking part in a research programme, co-ordinating a trial or running a tumour group has great educational value.

EORTC is a unique organization and there are a myriad of good reasons for joining its activities.