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European Charter on Obesity

An ambitious charter on obesity has been agreed by policy-makers in the World Health Organization (WHO) European Region. It sets the goal of curbing the epidemic and reversing the current trend, and declares "Visible progress, especially relating to children and adolescents, should be achievable in most countries in the next 4–5 years and it should be possible to reverse the trend by 2015 at the latest."

The European Charter on Counteracting Obesity was signed at a WHO European Ministerial Conference in Istanbul, Turkey, on 16 November 2006. It was signed by Dr Marc Danzon, WHO Regional Director for Europe, and Professor Recep Akdag, minister of Health of the Republic of Turkey, on behalf of the 53 countries in the WHO European Region.

Ministers of health and senior policy-makers from other relevant ministries adopted the Charter. They declared their commitment to strengthening action on counteracting obesity and placing the issue high on the political agendas of their respective governments.

The Charter calls for targeted action across many sectors and for a focus on children that encourages them to establish health habits early in life, and protects them from commercial influence.

Specific measures include:

- the adoption of regulations to substantially reduce the extent and impact of commercial promotion of energy-dense food and beverages, particularly to children, with the development of international approaches, such as a code on marketing to children.
- promotion of cycling and walking through better transport policies and urban design.
- promotion of breast-feeding.
- reductions in the amount of fat, sugar and salt in manufactured products.
- establishing opportunities for daily physical activity and for good nutrition and physical education in schools.

"We are all aware that obesity is one of the most serious public health challenges facing Europe today," said Dr Danzon. "Evidence exists on what needs to be done to reverse the trend. This Charter commits Member States to put obesity high on their political agendas and calls on all partners and stakeholders to do the same. It is a guide, an opportunity, and gives us the tools to take effective action."

TV Advertising Ban

Ofcom, the independent regulator of the UK's communications industries has decided to ban advertising of food and drinks high in fat salt and sugar "in and around all programmes of particular appeal to children under the age of 16, broadcast at any time of day or night on any channel."

The British Medical Association says this does not go far enough. "Some of the most popular programmes amongst the under-16s are soaps which will not be covered by this ban," said Dr Vivienne Nathanson, the BMA's Head of Science and Ethics. "Ofcom clearly believes that TV advertising has an effect on children's eating habits, yet it does not have the courage to recommend a more comprehensive ban."

Ofcom estimates that the impact of the ban on total broadcast revenues would be up to £39 million per year (Euro 26m), falling to £23m (Euro 15m) as broadcasters mitigate revenue loss over time.

Orphan Status for Leukaemia Drug

The European Medicines Agency (EMEA) has granted orphan drug designation to lestaurtinib (CEP-701) for the treatment of acute myeloid leukaemia (AML). The designation gives manufacturer Cephalon a 10 year period of marketing exclusivity once the compound receives marketing approval.

Orphan drug status is given to medicines intended to treat life-threatening diseases affecting less than 5 in 10,000 people in the European Union. Although 14,000 people are diagnosed with AML in Europe each year, only around 25–30 percent have the FLT-3 genetic mutation which is associated with poorer prognosis and survival.

Lestaurtinib inhibits several tyrosine kinases, including FLT-3. It is a targeted agent against AML in patients at first relapse from standard chemotherapy and whose disease presents with a FLT-3 activating mutation. It is in phase II and III clinical trials.

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Protoxins in Prostate Cancer

A novel protoxin, designed to be activated by prostate-specific antigen (PSA), is entering clinical trials amid hopes that it could become a highly specific treatment for prostate cancer. At the EORTC-NCI-AACR Symposium, Professor Sam Denmeade (Johns Hopkins University, USA) said, "This represents a different kind of targeted therapy, in that it seeks to use a protein made by the cancer to destroy itself."

He and his team modified an inactive proaerolysin to make the protoxin, called PRX302. It was engineered to be activated by PSA. Once activated, it kills the cancer cells by forming large pores in the cell membrane.

Initial work in animals has suggested that the agent causes little damage to surrounding tissues. In cynomolgus monkeys with PSA-producing prostates, a single injection of PRX302 destroyed up to 50% of the prostate tissue with no toxicity observed in other normal tissues such as bladder, urethra, rectum and seminal vesicles. The agent had disappeared 2 weeks after the injection but the dead tissue remained, suggesting, Professor Denmeade said, that the toxin's effects could be long-lasting.

Use of the protoxin is currently limited to men who still have prostates. A phase I clinical trial is in progress for men with locally recurrent prostate cancer after definitive radiation therapy. "If it were to work very well it might be used earlier, in combination with other treatments, most likely radiation. In addition, the toxin is also under consideration as treatment for benign prostatic hyperplasia. We hope that we will be able to further modify the toxin to make a systemic form that could be used to treat advanced prostate cancer in the future," Professor Denmeade said.

The third cohort of patients in the study is being treatment and interim results were expected at the end of 2006. (*Proc EORTC-NCI-AACR 2006 # 526*)

Relapse Prevention in ALL

Researchers have identified cells that cause relapse after treatment for acute lymphoblastic leukaemia (ALL). When these clones of the ALL cells are present, a patient will inevitably relapse after chemotherapy, no matter how well they responded initially.

Presenting new data to the EORTC-NCI-AACR Symposium on 'Molecular Targets and Cancer Therapeutics (Prague, Czech Republic, 7–10 November, 2006), Ms Seoyeon Choi (Children's Cancer Institute, Sydney, Australia) said that the clones have a pre-existing, rather than acquired, resistance to drugs used in treatment.

Nearly all ALL patients respond initially to chemotherapy, but one in 4 relapse. Ms Choi, a final year PhD student, said, "We have previously shown that these relapses were due to small numbers of surviving and highly drug-refractory cells. However, until now, it has been unclear whether these relapses resulted from the acquisition of therapy-induced drug resistance or were caused by a subpopulation of cells that were already intrinsically drug resistant."

Samples were taken from 25 patients at the time of diagnosis and at their relapse. Analysis of the lymphocytes revealed markers for new clonal populations at the time of relapse in 13 of the patients. In 8 of the samples, using polymerase chain reaction, Ms Choi found that these relapse clones had been present in small numbers at the time of diagnosis, indicating that they were involved in the mechanism of relapse.

"My research indicates that these are not different leukaemias, but a smaller population of related cells that are naturally more aggressive than the major clone. The problem is that they are present at such low levels, hidden behind the obvious leukaemia; the patient would appear to be responding well to treatment with the major leukaemia clones dying, but in fact, the small number of sub clones can survive therapy and cause a relapse," she said.

The presence of the sub clone at diagnosis correlated significantly with the length of the first clinical remission and the more of the sub clone that was present, the quicker the patient relapsed.

The discovery means that researchers may now be able to design therapies to specifically target these resistant sub clones so that in future, patients who have been identified as having them can be treated immediately with alternative therapies. (*Proc EORTC-NCI-AACR 2006 # 252*)

Inhibiting Aurora Proteins in Solid Tumours

Blocking aurora proteins – which play a key role in cell division – may be an effective way of treating advanced or metastatic solid tumours, say researchers from the Netherlands. Early results are "promising".

Aurora proteins belong to a family of enzymes which regulate division of the cell nucleus in mitosis. The proteins are overexpressed in cancer, which causes unequal distribution of genetic material between the two daughter cells. Abnormal cells – the hallmark of cancer – are created. Scientists have recently started to investigate the proteins as targets for anti-cancer therapies.

Dr Maja de Jonge (Erasmus University Medical Centre, Rotterdam) and colleagues conducted one of the first studies of an aurora kinase inhibitor in patients. They used PHA-739358, which was discovered and characterised by scientists at Nerviano Medical Sciences in Italy.

A phase I trial included 36 patients with a range of solid tumours. Above a particular dose level (190 mg/m^2), tests on skin biopsies showed that the drug interfered with cell division – and therefore that its mechanism of action was as predicted. "The clinical trial has proved the concept that inhibition of the aurora protein disrupts an important stage of cell division," Dr de Jonge told delegates at the EORTC-NCI-AACR Symposium. "Patients are able to tolerate the drug and dosing schedule, and it is exciting that, at this early stage in the drug's development, there is evidence of its ability to stabilise advanced disease." (*Proc EORTC-NCI-AACR 2006 # 27*)

EUROFILE

Transatlantic Cooperation on Intellectual Property

Intellectual property (IP) was high on the agenda at the second EU-US economic summit which took place in November, 2006. Enterprise and Industry Commissioner Gunter Verheugen and Mauri Pekkarinen, the Finnish Minister for Trade and Industry representing the EU Presidency, discussed IP issues with their US counterparts from the departments of the economy and energy.

The EU–US relationship encompasses €600 billion of trade in goods and services each year, large flows of investment and employment to 14 million people on both sides of the Atlantic. Strengthening the relationship between the EU and the US could translate into huge economic benefits and make both economies more competitive and dynamic, both sides said.

"The aim of strengthening growth and competitiveness, creating jobs and boosting productivity through innovation, lies at the heart of both the European economic agenda and of the transatlantic Economic Initiative," said Verheugen. "Results-oriented policies in the areas of innovation – which includes protecting and enforcing our intellectual property rights – and regulation will reduce bureaucracy and regulatory barriers to trade and investment. It will make a real difference for our citizens and our businesses on both sides of the Atlantic."

The EU and US agreed to support innovation in health care, nanotechnology and the automotive industry as part of the transatlantic innovation initiative, and to strengthen efforts to remove regulatory barriers to trade and investment. Following the adoption of a joint strategy to fight soaring global illegal trade in counterfeit and pirate goods, EU and US experts are working together to protect intellectual property rights (IPR).

At the EU–US education summit earlier in 2006, an action strategy for the enforcement of intellectual property rights was signed. A number of initiatives were also agreed, including fostering public-private partnerships to protect intellectual property, exchanging IPR border enforcement practices and experiences; and identifying specific areas for cooperation. The agreement also aims to promote public-private partnerships and involve small/medium enterprises (SMEs) in IPR protection.

In addition to the IP proposals, the summit agreed to promote long-term partnerships between European and American higher education institutions. The Commission will allocate €45 million to the programme, which runs until 2013. This will enable 6000 EU and US citizens to participate in mobility activities over the course of the programme. Planned actions include joint consortia projects, which will provide support for joint study programmes and exchange mobility projects to provide follow-up financial support for student mobility. Funding will also be used to support the development of transatlantic degree programmes, and policies to facilitate the sharing of best practice in higher education.

Worthy though these aims are, some wonder whether the EU should not be getting its own house in order first. A report published in September 2006 by an expert group of CREST, an advisory committee of research officials from EU member states, followed on from the long-running and finally stalled attempt to set up a single patent system for the whole of the EU. The report made up part of the "Open Methods of Co-ordination" project, which tries to help member states to work together on matters relating to IP. At the time Mike Edwards, a UK IP consultant and rapporteur for the project, said: "Issues relating to differences in the way intellectual property is treated from country to country are not really a problem as long as people are aware of them and how to get around them. They don't present an obstacle to cross border collaboration."

''THE EU SHOULD GET ITS OWN HOUSE IN ORDER FIRST''

Gilles Capart, chairman of ProTon Europe, the pan-European network of technology transfer offices linked to universities and public research institutions, was critical of this approach. It was 'disappointing', he said, that the report had avoided making recommendations on how to move forward with harmonising IP regulation across Europe.

Some member states are making overtures to other countries in a bid to help both themselves and countries such as China and India, where IP and product piracy are already causing problems. In July, 2006, France and India signed an agreement to promote co-operation in IP. Both countries will share best practice on intellectual property rights and will carry out bilateral studies on various aspects of IP, to be administered by the French National Institute for Intellectual Property and the Indian Department of Industry Policy and Development.

"In a globalised world, where bilateral commercial exchanges are growing, it is essential to have in-depth discussions on intellectual property, notably best practice. This will help to ensure a favourable environment for industrial affairs and the economy," the French and Indian ministers said in a statement.

''IS OPEN INNOVATION AT ODDS WITH IP PROTECTION''

The WHO adopted a report in May, 2006, that said patent protection was not driving innovation in a way that would allow poorer countries to have access to essential medicines. With this, who knows what will happen next? The push for collaborative and open innovation seems strong, and it comes not just from developing countries. Are such systems at odds with intellectual property protection? And does that matter if those creating the innovation want to make it widely available? These are some of the questions that are bound to be raised by the European Parliament when the Community Patent comes up for discussion in the future.

Mary Rice
Brussels

Health Migration and Childhood Cancer

Major inequalities exist in cancer care between the western European states, emerging Balkan Member States, and countries outside Europe in Asia and Africa. Coupled with the expansion of Europe in the past decade and a general increase in global mobility, the inequalities have promoted a health migration, in which patients travel to other countries for treatment.

Paediatric oncology is one specialty in which inequalities in treatment success are especially evident. Eva Steliarova-Foucher (International Agency for Research on Cancer, Lyon, France) reports that in a number of studies published in September, 2006, several countries from eastern Europe showed 5-year survival that was lower than that in other European countries. (*Eur J Cancer* 2006;**42:***1913–2190*).

Gordon McVie, European Institute of Oncology, Milan, Italy, agrees. "The cure rates for some paediatric leukaemias are around 90% in the UK, and this is in stark contrast with African countries,

''THE TIME AND EMOTIONAL INVESTMENT MAY BE EVEN HIGHER THAN USUAL''

where the disease is 90% fatal. The emerging Balkan states fall somewhere between these two extremes but the prospect of parents migrating to save the life of their child is understandable", comments McVie. He points out that the first cases of health migration of children for cancer care occurred after Chernobyl, when children with thyroid cancers and leukaemias moved to the UK for treatment. "The UK government was able to fund this but only because the number of children involved were finite. The number of children with cancers is, thankfully, low, but not finite and the financial implications of continuing health migration must be addressed", he says.

The pressure on oncologists also needs consideration. Luisa Massimo (G Gaslini Children's Research Hospital, Genova, Italy) reports that language and cultural difficulties are major hur-

''EACH EASTERN EUROPEAN COUNTRY COULD HAVE A CENTRAL INSTITUTE''

dles to instigating and completing treatment. An African child with abdominal rhabdomyosarcoma (RMS) was referred to her clinic in 2000; neither the child nor her father could speak Italian and no common language or interpreter could be located. "Obtaining informed consent for the treatment was difficult; eventually, some communication via a nun with some knowledge of the African language enabled us to have the illiterate father make his mark on a consent document, which satisfied the then standard European RMS protocol", she explains.

Roberto Labianca (Hospital Riuniti, Bergamo, Italy) has also had language difficulties with migrant patients and cultural differences in the way people cope with cancer. "This puts pressure on the teams as time and emotional investment for such patients tends to be even higher than is usual", he comments. Labianca is Chair of the Task Force behind the Medical Oncology Status in Europe Survey report, which analysed data from 34 countries to investigate discrepancies in practice between European and developing countries. "We found wide differences in the teaching of oncology, organisation of oncology, and multidisciplinary team use", summarises Labianca.

With the acceptance of Romania and Bulgaria into the European Union in January, 2007, and the prospect of Turkey being eligible in a few years, migration could become more of an option for these countries. "Health migration from Hungary to western European countries has not had a great impact since our entry into the EU in 2004 but there is a potentially more serious emerging problem due to the health migration to Hungary from Romania and Ukraine, where the healthcare systems are less developed than in Hungary", reports Dezsõ Schuler (Semmelweis University, Budapest, Hungary). He stresses that although cancer survival is somewhat lower in Hungary than in western European states, the gap is closing. "It will be possible for Hungarian health institutes to deliver the same quality of treatment as the west, but it cannot happen at the moment", he says.

Hungary has difficulties with late diagnosis (because of poor public awareness of childhood cancers), limited access to care (because of logistic and financial issues), and poor infection control during treatment, but Schuler thinks that one possible way forward is to establish one central paediatric oncology institute in each eastern European country. These centres could be covered partly by a European budget to enable a good and fast referral system to local expertise. Training for general physicians and health visitors, and an education programme for the general public are also priorities, he says.

"From a humanitarian point of view, few people would try to stop this type of migration if cancers are diagnosed in time; childhood cancer is rare and there are hardly large numbers and the good cure rate means that mobility would save lives reliably", says McVie. However, he agrees that making migration easier is not an effective long-term solution: "It would be better to encourage the mobility of oncologists [and] make European funds available for doctor training and instruction, and improvement of facilities in countries where they are lacking", he concludes.

Kathryn Senior
This story originally appeared in Lancet Oncol 2006 **7:** 889.

Posaconazole approved

The European Commission has granted marketing approval to posaconazole (Noxafil) for prophylaxis of invasive fungal infections in patients at high risk. It covers patients receiving remission-induction chemotherapy for acute myelogenous leukaemia (AML) or myelodysplastic syndromes (MDS) expected to result in prolonged neutropenia, and haematopoietic stem cell transplant recipients who are undergoing high-dose immunosuppressive therapy for graft versus host disease.

It is also approved as first-line therapy for oropharyngeal candidiasis in patients who have severe disease or are immunocompromised, in whom response to topical therapy is expected to be poor.

PODIUM

Towards Recognition for Surgical Oncology

Professor Irving Taylor

Irving Taylor is professor of surgery and vice dean at University College London, UK. He has an interest in surgical oncology, in particular colorectal cancer and colorectal liver metastases. He is President of the European Society of Surgical Oncology and a past President of the British Society of Surgical Oncology.

How far is it possible for surgeons to specialise in cancer?
Many of us with a particular interest in surgical oncology deal with one or 2 types of malignancy, but also with many patients who have no malignancy. We are unlike other cancer specialists such as radiotherapists who only see people once malignancies have been diagnosed. We see patients referred with symptoms the GP thinks might be malignant. For many solid tumours, surgeons are the patients' first contact and often the individual to whom the patient becomes emotionally attached. We go through the full diagnostic panoply and those patients who don't have malignancy are still treated by us. A patient with rectal bleeding may have piles or rectal cancer but we treat both; we are trained to do so. Once cancer is diagnosed, patients are seen in a multidisciplinary setting, but somebody has to see them first.

Would you like to see more specialisation?
It is difficult to say yes. In the UK and most of Europe, there are only a very few cancer hospitals where patients are referred after a cancer diagnosis. The majority of hospitals deal with the whole range of patients. It is quite routine – and probably better – for cancer patients to be in an environment where others have different conditions, as long as the individual surgeon has expertise in their particular malignancy. To get good results, surgeons have to maintain their experience and skill levels by dealing with a certain number of patients per year, and work in a centre with specialist facilities for diagnosis, intensive care, pathology, and so on. This is a requirement for true specialisation.

But surgical oncology is not a recognised specialty?
In the UK, there are 9 surgical specialties such as general surgery, orthopaedics, plastic surgery etc and each includes the surgical management of cancer. But, in most of Europe, surgical oncology per se is not a recognised specialty.

Why would you like it to be recognised?
Surgical training differs throughout Europe but most European countries have a one or two year period of basic surgical training, followed by specialist training, for usually 4 to 5 years. Each specialty inevitably includes oncology so most surgeons deal with cancer to a certain extent in their training. But there is no recognised programme by which a surgeon specialises in cancer to the exclusion of all else.

There is a role for surgical oncologists with a detailed awareness of the pathology and natural history of the disease, imaging techniques, and so on. You could expect this training to improve outcomes. ESSO has put together a surgical oncology curriculum, available on the ESSO website, which pulls together different facets of oncology important for cancer surgeons to be aware of, and details the specialisms an individual needs to expand an interest in oncology. The syllabus is both generic – including an understanding of the molecular biology of cancer, or different investigations – and also specific to a particular organ.

Does ESSO advise on the minimum number of cancer cases surgeons should have?
There are guidelines for all malignancies. It is becoming increasingly obvious that to get the best results in terms of survival and local recurrence rates, individual surgeons should be doing a certain number of cases. The volume is important but so is specialisation. In 1990, a woman with a breast lump, for example, would have gone to a general surgeon, who might not necessarily have had a breast specialism. Now she is directly referred to a specialist in breast disease.

Is there any downside to increasing the emphasis on surgical oncology as a specialism?
It's a balancing act, there are disadvantages. Surgeons see a more restricted range of cases which can sometimes reduce job satisfaction. In addition they may involve themselves less in emergency work, for example. Further, if everyone specialises, more consultant surgeons will be needed and so healthcare will be more expensive.

What do you hope to achieve at ESSO?
We will continue to run educational courses and meetings and we set a European examination in surgical oncology which is taken by trainee surgeons each year. We want to increase European collaboration particularly in randomised clinical trials and we support European fellowships for surgeons to visit major centres and learn specific techniques.

At meetings, we encourage surgeons with different areas of oncological interest to discuss common problems. I would like to encourage organ-based surgical societies with major oncological interests to collaborate with ESSO, so that surgeons in all specialties can form close links and exchange good practice when dealing with patients with solid malignancies.