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NEWS...NEWS...NEWS

EU Directive begins to bite

The widely-criticised EU Clinical Trials Directive has been hindering research in the months since it came into force, according to the SaveEuropeanResearch.org campaign. Campaigners are gathering evidence to strengthen the case for an early review of the Directive.

Dr. Brian Moulton (Irish Clinical Oncology Research Group, Ireland) said that, as expected, clinical trial applications in Ireland rose slightly before the Directive came into force. However, in the 4 months preceding the Directive, applications were up only 20% (compared to the average for 2002); they were down 50% in the 4 months after it came into effect.

At the EORTC, two trials (protocols 5501 and 24021) aimed at reducing the extent of surgery in vulva cancer and oropharyngeal squamous cell carcinoma, respectively, have not been started. The trials, intended to reduce post operative morbidity, had been peer reviewed and accepted scientifically, but can not go ahead because of a lack of financial support to cover the extra administration required by the new regulations.

The Milan Institute of Oncology had the cost of a clinical insurance policy increased from €13,000 in 2003 to €108,000 in 2004 as a result of the insurance company's perception of its increased responsibility as sponsor under the Directive.

''A CLINICAL INSURANCE POLICY INCREASED FROM €13,000 TO €108,000''

Sirtex Medical Ltd., an Australian biotech company has indicated in writing that it will be moving its latest phase of clinical trials out of the EU because of the increased costs directly attributable to the Directive.

However Dr. Patrick Therasse at EORTC, said that a forthcoming EU Directive on Good Clinical Practice (GCP) may help. ''The Commission seems to be open to integrating specific modalities for non-commercial research in the coming Directive (indirectly correcting some inconsistencies from the earlier Clinical Trials Directive), but I understand it may be difficult to convince national authorities to accept this. We may need to create some more public noise as we did some time ago to attract the attention of our politicians''.

The Commission held a meeting in November, 2004, involving representatives of all parties interested in non-commercial research. Afterwards, Dr. Therasse wrote to Dr. Birka Lehmann, who is responsible for the GCP Directive at the European Commission. The letter addressed the definition of non-commercial trials and access to marketed drugs, the definition of investigational medicinal products (IMP), problematic details in the ICH (International Conference of Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) GCP in the context of non-commercial trials, and the application for authorisation of clinical trials.

A further meeting involving member state representatives was due to take place in December, 2004.

The SaveEuropeanResearch.org campaign is asking researchers to send on further verifiable examples of research impeded by the Directive. (Contact brian.moulton@icorg.ie)

Towards worldwide cervix screening

A consortium of international public health agencies has launched a 'toolbox' for worldwide implementation of effective screening programmes for cervical cancer.

The consortium has produced *Planning and Implementing Cervical Cancer Prevention and Control Programs: A Manual for Managers* which, according to International Agency for Research on Cancer (IARC), can be directly included in countries' public health strategies. The manual provides information on how to plan, establish, implement, strengthen and monitor cervical cancer prevention and treatment services, recognising that various service delivery options are needed for different geographic and cultural settings and a range of resource levels.

International studies have shown that, if well-organised and monitored, low-frequency cervical cancer screening programs are cost effective in many low-resource settings. Despite this, few exist. Dr. Peter Boyle, IARC Director, said, ''Cervical cancer is undoubtedly a public health issue that can and needs to be remedied by building awareness, developing policies and implementing effective screening programs, recognising that screening is just the first step in the management of a woman with cervix pathology''.

A pdf version of the manual can be downloaded from
www.iarc.fr/ACCP/ACCP_screen.pdf

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The latest from ATAC

The latest results from the ATAC trial (Arimidex, Tamoxifen, Alone or in Combination) suggest that anastrozole should replace tamoxifen as the treatment standard for postmenopausal women newly diagnosed with hormone-receptor-positive early breast cancer.

The results were presented at the 27th Annual San Antonio Breast Cancer symposium (December 8–11, 2004), and published online at *http://image.thelancet.com/extras/04let11120web.pdf.*

Almost all of the 9366 women in the trial have now completed the standard 5 years of therapy, and median follow-up is 68 months. Compared with tamoxifen, anastrozole significantly prolonged disease-free survival (575 events with anastrozole *vs.* 651; hazard ratio HR 0.87). Anastrozole prolonged time to recurrence (402 *vs.* 498, HR 0.79) and significantly reduced distant metastases (324 *vs.* 375; HR 0.86) and contra lateral breast cancers (35 *vs.* 59, 42% reduction).

Professor Anthony Howell, Chair of the ATAC Steering Committee, said, ''This is the most compelling evidence that we have seen, so far, to indicate that anastrozole can replace tamoxifen as the treatment standard, to protect women from a potentially fatal relapse of their breast cancer''.

Over the 5 year period, anastrozole was significantly better tolerated than tamoxifen and no new safety concerns were raised. Women treated with anastrozole had more bone fractures than those on tamoxifen, but a lower risk of strokes, endometrial cancer and thromboembolic events.

The authors say that the results are only applicable to anastrozole ''since it is unknown how differences between the aromatase inhibitors affect their clinical usefulness''. It is ''reasonable'' to switch patients currently on tamoxifen to an aromatase inhibitor

''ANASTROZOLE SHOULD BE THE PREFERRED INITIAL TREATMENT''

and it is ''not appropriate'' to wait 5 years to start an aromatase inhibitor. ''5 years of anastrozole should now be considered as the preferred initial adjuvant endocrine treatment for postmenopausal women with hormone-receptor-positive localised breast cancer'', they conclude.

Art in oncology

On Hearing the News (*La Noticia*) by Catalina Aroch Fugellie.

This is the winning entry of an international art competition *Oncology on Canvas: Expressions of a Woman's Cancer Journey*, sponsored by Lilly Oncology. The competition was open to women from around the world diagnosed with cancer, their families and friends, plus involved healthcare professionals.

Catalina Aroch Fugellie's entry was considered by the judging panel to most effectively portray a woman's cancer journey in a way that inspires others to follow. She said, ''Oncology on Canvas has provided me the opportunity to share my feelings about my fight against cancer with others through art. I hope that my artwork will help inspire others who are facing a similar struggle''.

Increasing cancer rate in European children

The incidence of cancer among European children has increased year on year since the 1970s. The trend is significant and accelerating, say researchers from the International Agency for Research on Cancer (IARC).

Project co-ordinator, Dr. Eva Šteliarová-Foucher (IARC) said, ''Our results provide clear evidence of an increase in cancer incidence in children and adolescents over the past decades, and of an acceleration of this trend. However, cancer at these ages remains a rare disease''.

This is the first report of the European Union-supported ACCIS project (Automated Childhood Cancer Information System), a collaboration between 80 population-based cancer registries (*Lancet* 2004, **364**, 2097–2105).

The increases in incidence were seen in all ages, but were greater in children under 4 years, and in adolescents. In children, the average cancer incidence rate was 118 per million in the 1970s; 124 in the 1980s; and 139 in the 1990s. This increase, of 1% per year on average, was based on 100,596 children with cancer.

In adolescents, based on 15,460 adolescents with cancer (aged 15–19 years), the rates increased by 1.5% per year on average. Incidence rates per million were 147 in the 1970s; 165 in the 1980s and 193 in the 1990s.

All types of cancer increased in both children and adolescents. Leukaemias and brain tumours are the most common childhood cancers in Europe, while carcinomas and lymphomas occur most frequently in teenagers.

However, survival has improved dramatically since the 1970s. Then, 5-year survival was 44% for children and 50% for adolescents. In the 1990s, 5-year survival among children was 75% in western, and 64% in eastern Europe. Among adolescents the figures were similar.

Improvements in diagnosis and registration may explain some, but not all of the increases in incidence. The authors wrote, ''To follow up our important findings, it will be necessary to identify the specific tumour types and population groups that are specifically affected by these unfavourable trends and to try to establish their reasons''.

The peak in lymphoid leukaemias in early childhood may be a useful target for research. Both genetic and environmental determinants appear to play a role: the peak was more pronounced among those of European than of Asian or African descent, and within populations of similar ethnic origin, it was more pronounced in more affluent groups.

Improvement of socioeconomic status, increased population mixing or lack of exposure to certain viruses are potential explanations, the researchers say.

An accompanying editorial says that the ACCIS project represents 30 years of data collection and ''highlights the importance of population-based cancer registries in measuring cancer incidence, survival, and mortality''.

EUROFILE

Introducing Janez Potočnik

Janez Potočnik, former minister for European Affairs in Slovenia and the head of the negotiating team for Slovenia's accession to the EU, took up the post of Research Commissioner at the European Commission in November, 2004. At his hearing before the Industry and Research Committee he was praised by MEPs for his honesty, vision, and ability to admit when he did not know something – something many would say is rare in a politician. Clearly excited about his appointment, he talked to EJC's Mary Rice about how he sees his job and the future of European research.

Janez Potočnik, New Research Commissioner.

Was it the job you wanted?

As my country's nominee for European Commissioner, I was happy to fit into the Commission President's team as he saw best. I am certainly very pleased to have been entrusted with the Science and Research portfolio – it is an area of huge potential, fundamental to the achievement of the goals that Europe has set itself in terms of growth, competitiveness and employment.

Philippe Busquin had pretty strong ideas about the future of European research. Some people might consider this a hindrance to a successor. How do you see this?

I see this as a very good thing – it means I have a solid basis to build on. Mr. Busquin worked extremely hard for European science and research. He laid the groundwork for the major issues for the future: the 7th Framework Programme, the proposed increase in the research budget. I certainly intend to carry on this work to see these priorities through.

Cancer is on the increase all over the world, but particularly in developed areas such as the EU. Do you think that EU science is well enough funded and organised to be able to make a real impact on this disease? What more could be done?

Cancer is undoubtedly one of the major issues of public health today. It is therefore one of the main research issues to address. For this reason, cancer ranks among the top priorities of the current Sixth Framework Programme. With more than €400 million for four years, cancer research receives more funds at EU level than any other health problem. And there are successes: in fact, one of the Descartes Prize finalists this year was a team developing new diagnostic tools.

Europe as a whole – so beyond just the Framework Programme and including national programmes – devotes a lot of resources to cancer research, research aimed at developing new drugs, new screening and diagnostic tools and new treatments. The problem is that these important efforts remain largely uncoordinated. What we are doing at European level is to try to make the best possible use of European human and material research potential, by taking full advantage of the added value of actions at European level.

The various ''Networks of Excellence'' and ''Integrated Projects'' funded through the 6th Framework Programme in the cancer research area represent an important step in this direction. The focus is presently on so-called ''translational'' research, aimed at bridging basic and clinical research. More could be achieved by devoting further attention to European needs in terms of basic resources for cancer research (data bases and collections of living material, for instance), as well as to clinical applications.

How should decisions be made on which branch of science to fund? Sometimes one disease needs to be prioritised over another. How should this be done and by whom?

This is of course a very complex and delicate issue. Diseases are numerous, suffering is high everywhere, but money will always remain limited. How to make the right choices? A first option would consist of not making choices at all, by spreading funding equally across diseases and research subjects. It would remove the problem but not really solve it. But as policy-makers, we have responsibilities, choices must be made.

continued overleaf

Janez Potočnik at a glance:

2004 -	European Commissioner
2002 - 2004	Minister for European Affairs for Slovenia
1998 - 2004	Head of Negotiating Team for the Accession of Slovenia to the EU
2001 - 2002	Minister Councillor at the Slovenian Prime Minister's Cabinet
1993 - 2001	Director at the Institute of Macroeconomic Analysis and Development in Ljubljana
1988 - 1993	Senior Researcher at the Institute for Economic Research in Ljubljana
1984 - 1987	Assistant Director at the Institute of Macroeconomic Analysis and Development in Ljubljana

Education

1993 Ph.D. in Economics, Faculty of Economics at the University of Ljubljana

Janez Potočnik was born on 22 March 1958. He is married and has two sons.

Radon and lung cancer risk

Radon gas in ordinary homes across the country increases the risk of lung cancer, particularly among smokers, researchers say. It is responsible for approximately 20,000 lung cancer deaths in the European Union each year (*BMJ, doi:10.1136/bmj.38308.477650.63 (published 21 December 2004)*).

The study – funded by Cancer Research UK and the European Commission – was a collaborative analysis of individual data from 13 case-controlled studies of residential radon and lung cancer. Radon gas concentrations were measured in homes inhabited during the previous 5–34 years. The study included 7148 cases of lung cancer and 14, 208 controls.

Lung cancer risk increased by 16% per 100 Becquerel/cubic metre increase in usual radon. The dose-response relation seemed to be linear with no threshold and remained significant in analyses limited to people from homes with measured radon <200 Bq/cubic metre, which is the currently recommended 'action level' in the UK. Indeed, the researchers estimated that about 90% of radon-induced lung cancers occurred in homes with levels of radon below 200 Bq/cubic metre.

In the absence of other causes of death, the absolute risks of lung cancer by age 75 years at usual radon concentrations of 0. 100 and 400 Bq/cubic metre would be about 0.4%, 0.5% and 0.7%, respectively, for lifelong non-smokers, and about 25 times greater (10%, 12% and 16%) for cigarette smokers.

Professor Sarah Darby (University of Oxford, UK) led the study and said, ''We have shown that radon in ordinary homes is causing about 9% of lung cancer deaths each year in Europe, which is about 2% of all cancer deaths''.

Radon is formed from the natural disintegration of uranium, which is present in ordinary surface rocks and in soil. Radon that diffuses into the atmosphere usually disperses rapidly but it can accumulate indoors. As radon decays it creates particles that can damage the cells lining the airways of the lungs.

High radon levels in existing houses can usually be reduced by changes to the ventilation system. Professor Darby said, ''Over the next few decades one of the most cost-effective ways of reducing the number of lung cancer deaths caused by radon may be for builders to incorporate low-cost radon-proof membranes into the foundations of all new homes, even in areas that are not currently designated as being particularly radon-affected''.

Janez Potočnik (continued)

A traditional and appropriate criterion for justifying public funding is the degree to which it allows the correction of ''market failures'': all things being equal, priority should be given to research on diseases (or to aspects of such research) which will not benefit substantially from private efforts. In this respect, research on ''rare diseases'' and ''poverty-related diseases'' are two of the best cases for public funding.

The main justification of EU research funding is always its ''added value'' in comparison with national efforts. In the case of cancer, we can see that there is already significant funding across Europe. So in this field, European ''added value'' lies in increasing the co-ordination of research activities, establishing common ''soft infrastructure'' usable by many research communities and benefiting from the statistical advantages of working at European scale, as well as for dealing with populations with diverse food habits and living conditions. It will also be important to continue investing in basic research, which could further our understanding of the causes of cancer. But these arguments apply to many diseases. So priority choices will always be difficult.

Busquin was on the record as saying that he would involve civil society in decisions on which research to fund and the overall direction of research under Framework 7. Do you think this is realistic and good for science, and if so,how do you see it proceeding? Should patients be more involved in deciding on research for their conditions and how?

We need to be closer to the citizen in all matters of research. We should be aware of what their concerns are, and work better at informing them of the importance of science and research for their quality of life. For health and medical issues, we certainly value the input of patients. Looking at health and medical research in particular, patient associations for a given condition provide valuable information about quality of life issues, and are already playing a significant role in the implementation and, to a certain extent, the definition of research activities.

There has been much talk about the Lisbon agenda and EU/US competitiveness. How do you see the situation evolving over the next ten years?

Undoubtedly, the current situation is that unless the EU takes action quickly, we will have no chance of reaching the targets we set for ourselves for 2010. The recent report by Wim Kok backed this up. What is clear is that we need to put knowledge right at the top of the agenda – knowledge is central to securing EU competitiveness and sustainable economic growth. Generating new knowledge through research, exploiting it in industry through innovation, disseminating it via education, training, mobility of people, technology transfer – these are issues that are the lifeblood of our economy and our society. So for me, what is needed is a renewed and enhanced commitment to research, innovation and education.

In many European countries, there are quite strong anti-science sentiments which can hamper those trying to do important research. Do you see this situation changing? If so, where and how?

An issue we are up against in the science field is this one of public perception. I see this as something to be addressed from several different angles. We should communicate about science and research in a way that engages the public's interest, and shows them how they benefit on a daily basis from what is being done in the world of science. A crucial aspect is capturing the interest of young people – the scientists of the future. Children are naturally great innovators, and are curious about how the world around them works. Somewhere along the line that curiosity and inventiveness is lost. So we should look at how science is explained and taught to children, with a view to encouraging more children to get involved.

What do you hope to achieve in your term, both pragmatically and idealistically?

There are various milestones that are identified for my term in office – the establishment of the 7th Framework Programme, the new budget period, where the Commission has proposed injecting more money into research, innovation and competitiveness. But these things contribute to the same central goal, which is to put knowledge at the heart of our political and economic thinking. I hope that at the end of 5 years, we will be closer to achieving that.

Interview by Mary Rice, Brussels

PODIUM

ECCO: a showcase for the future

Prof. Harry Bartelink (Netherlands Cancer Institute, Amsterdam) has research interests including prediction of treatment outcome with micro-arrays in breast cancer patients; high dose-high precision radiotherapy; quality assurance. He is honorary fellow of the American College of Radiology, ESTRO Breur Medallist and a past President of ESTRO. He is President of FECS and of ECCO-13 (Paris, 30 October–3 November, 2005)

Professor Harry Bartelink

Tell us about ECCO-13

ECCO-13 will have a different format which originated from a change in the composition and structure of the scientific committee, to include more topic-orientated clinicians and scientists. We will devote more attention to translational research. This meeting is taking place at the right time; more new agents have been developed as a result of basic research into the mechanisms of cell death, pathways, and so on. At ECCO-13, presentations of new data will demonstrate that fundamental research has led to new drugs which are effective in the clinic.

We have been waiting a long time for these results?

We should not underestimate progress made in new technology over the last few years. For example, it is now clear that microarrays can predict the course of disease, and tell us whether patients will die from the primary tumour or distant metastases. Small interfering RNAs (siRNAs) can silence certain genes in cells and animals. Both methods will in future allow us to predict in advance which patients will respond to a particular drug – a major step forward. ECCO will include presentations of recent examples.

What other themes will be apparent at ECCO?

ECCO is a multidisciplinary meeting and many symposia will include speakers from all different fields – basic research, diagnostics, pathology, radiotherapy, surgery, chemotherapy. This is in line with what is happening in hospitals, different disciplines are working together in teams.

But many still feel a strong allegiance to their speciality?

People grow up within a discipline, so there is a loyalty. But this is changing in the clinic. The UK for example has seen a reduction in breast cancer mortality due to multidisciplinary working and better integration of diagnostics, radiotherapy, surgery, and so on. Increasingly across Europe, we see closer cooperation between the different specialists treating an organ-specific cancer – colorectal or breast cancer, for example – than within each discipline.

How are individual disciplines catered for at ECCO?

We have not forgotten the disciplines; every day each speciality will find something of specific interest. But even here the multidisciplinary approach is emphasised, so there might be a section on chemotherapy specifically for surgeons, for example.

Overall, what do you want ECCO-13 to achieve?

We want to take ECCO to a higher level both for education and science. We want to have presentations of the first results from major clinical trials. We already have leading phase III trials lined up, but we want more results to be presented for the first time at ECCO. Especially those in translational research. We want to show that there is no need to go to the US because results are being presented in Europe first.

Is not it important for researchers to present in the States?

It's more important to publish in a leading journal. In radiotherapy, its already true that research is often presented first in Europe, but it's different in medical oncology and we want to change that.

How far do the aims of ECCO tie in with the aims of FECS?

The basic aims of FECS include the multidisciplinary approach, and the movement of translational research into the clinic, which will be reflected strongly at ECCO. There's also a political dimension. We are working on creating a stronger identity for oncology, so that we can defend the needs of patients. We want to make it clear to politicians at European and national levels that we – doctors, researchers, nurses, patients themselves – are fighting for a better future and better treatment for cancer patients. A special patient program will address these issues.

What are FECS' current campaigns?

FECS has been extremely active in trying to modify the rules of the European Clinical Trials Directive – a major task in itself – but we want to have more impact on future decisions from the European Parliament. Issues include availability and standards of care. We foresee a fantastic opportunity as new, effective drugs come on to the market, but they will be expensive and could consume a large part of countries' budgets. It will create problems and these drugs need to be introduced carefully. Another issue is European enlargement. We would like to see equal access to the best treatment for all patients no matter where they live. In practice, that means producing minimal standards for surgery, chemotherapy, radiotherapy and all specialists for all European countries.

FECS is an umbrella organisation and facilitates interaction between different societies. Oncology is still too fragmented but FECS is bringing the multidisciplinary approach seen in the clinic to a political and structural level. By joining forces we will be more effective than in the past. This is the aim of a strategic meeting organised by FECS in January 2005.