ELSEVIER

available at www.sciencedirect.com

SCIENCE DIRECT®

journal homepage: www.ejconline.com

NEWS. . .NEWS. . .NEWS

ESMO withdraws from FECS

Many European cancer specialists have greeted with dismay the decision by the ESMO Executive Committee to withdraw from all FECS activities. They fear that it could set back the cause of multidisciplinary research and treatment for years to come.

The decision was communicated to FECS in a letter late in 2005 from the outgoing ESMO President, Dr. Paris Kosmidis (Hygeia Hospital, Athens, Greece). The reasons given were FECS' announcement that it will not become a member-based society, along with the federation's inclusion of organ-based societies as FECS full members.

The letter stated that the decision was taken "in the interest of the profession of medical oncology and oncology in Europe, and according to the decisions taken during the 2005 ESMO General Assembly". However, ESMO members say they have yet to be officially informed.

The current ESMO President, Professor Håkan Mellstedt (Karolinska University Hospital, Stockholm, Sweden) defended the decision, and insisted that the aim was to create a single European society for oncology. He said that a member-based society was important to ensure a democratic process within the organisation, and that organ-based societies, which include professionals whose main focus of work is not oncology, should not be able to influence a European cancer society.

FECS' view – and that of many cancer specialists, including medical oncologists – is that the practice of cancer medicine and the organisation of cancer research is reflected by organ-based activities: breast cancer clinics, colorectal cancer clinics and so on. In a letter to industry explaining FECS' new position, FECS President, Professor John Smyth (University of Edinburgh, UK), said, "The new Societies which have emerged to represent these organ-based activities are a major part of the European landscape and the Federation wishes to expand to embrace our colleagues across the entire spectrum of cancer management and research. This also includes patients and their representatives".

''WE HAVE TO JOIN FORCES. IT IS A FACT OF LIFE''

Professor Mellstedt said that the "overwhelming majority" of responses to the decision were positive, in particular those from non-European members. One-third of ESMO's members are from outside Europe, especially from the US, Australia and Asia. "It is very important that we listen to what they are saying", he said. But medical oncologists who object to the decision questioned the relevance of these views. "ESMO is supposed to represent European medical oncologists", said one.

Within Europe, Professor Mellstedt said, there was a geographical divide in the responses, with southern Europe more in favour and the most vociferous objections coming from the UK and Benelux countries. One reason for the difference in response could be the status of medical oncology. Medical oncology is acknowledged as a specialty throughout much of northern Europe, where it remains part of general medicine in many of the Mediterranean countries.

Other specialties have expressed concern. The President of European Society for Therapeutic Radiology and Oncology (ESTRO), Professor Michael Baumann (University of Dresden, Germany), said he was "very sad" about ESMO's decision. "The future of oncology is interdisciplinary. We need to join forces. Oncology has to make its point compared to other specialties such as cardiology and things other than medicine which require resources. We can't afford to have 20 voices all claiming to speak for oncology in Europe. We have to sit down together and work out what is best for patients, researchers, clinicians and so on, then speak to politicians and providers of healthcare with one voice. If we don't do that, we will waste a lot of time and that can't be good for patients" (*and see Podium, page 807, this issue*).

''IT WILL BE A NEW MULTIDISCIPLINARY SOCIETY''

The way ahead is uncertain. Some medical oncologists object so strongly to the move that they are considering resigning their membership of ESMO. Should that happen in large numbers, it would create a gap for an alternative society for European medical oncologists. Alternatively, disaffected ESMO

(continued on next page)

doi:10.1016/j.ejca.2006.03.005

(continued from previous page)
members might choose instead to join ASCO (American Society for Clinical Oncology). Clearly, neither of these outcomes would promote unity in Europe.

The proposal by the Executive Committee that ESMO should change its name from European Society for Medical Oncology, to European Society for Multidisciplinary Oncology, was rejected out of hand by ESMO members at their General Assembly during ECCO 13.

Professor Mellstedt insisted that negotiation and compromise is the way ahead. But surely surgeons, radiotherapists and other cancer specialists are unlikely to join ESMO? "It will not be ESMO, it will be another, new, multidisciplinary society. That is very important", he said.

Doesn't ESMO's withdrawal from FECS put the organisations in direct competition with each other? Professor Mellstedt: "We don't see this as a competition. This is a discussion period. We are trying to find a way for oncology in Europe to be organised in future. We are having discussions with other organisations, including FECS. At the end of the day, we will find a solution".

FECS is also being conciliatory. The President's letter said, "We are greatly saddened that ESMO feel challenged by this modernisation of FECS and we hope to continue dialogue with them so that they will feel able to be partners in the future organisation, not only of conferences but also the overall development of cancer services throughout Europe".

Medical oncologists objecting to ESMO's move insist that the only way forward is for ESMO to cancel its decision and for discussion to start again. "We need truly multidisciplinary discussions with FECS as the platform. If that doesn't happen, there will be a split in medical oncology in Europe. That's the concern. We were at the stage of uniting oncology in Europe. This move is very harmful".

Professor Baumann is more optimistic and hopes that ESMO's decision can be reversed. "I believe that, in the end, reason will prevail. We have to join forces. It is a fact of life".

Positive opinion for clofarabine

Clofarabine (Evoltra) has received a positive opinion from the European Medicines Agency (EMEA) for the treatment of acute lymphoblastic leukaemia (ALL) in paediatric patients who have relapsed or are refractory to at least two prior regimens, and where there is no other treatment option anticipated to result in a durable response.

The positive opinion to the marketing authorisation application was adopted by EMEA's Committee for Medicinal Products for Human Use (CHMP) at its meeting in February 2006. It will take up to 3 months to be converted into marketing authorisation by the European Commission.

Clofarabine, produced by Bioenvision, is a "next generation" purine nucleoside analogue, and the company says the drug is in clinical development for numerous other diseases. These include acute myeloid leukaemia (AML), myelodysplastic syndrome (MDS), chronic lymphocytic leukaemia (CLL), chronic myeloid leukaemia (CML), non-Hodgkin's lymphoma (NHL), multiple myeloma, solid tumours and as a preconditioning regimen for transplantation.

The drug has been granted orphan drug designation for the treatment of both ALL and AML is the US and Europe. In Europe, the designation provides marketing exclusivity for 10 years following marketing authorisation.

Orphan status for glioma drug

The European Commission has granted orphan designation for enzastaurin hydrochloride in the treatment of glioma. The drug is an oral serine–threonine kinase inhibitor, designed to suppress tumour growth via several mechanisms. Manufacturer Eli Lilly and Co., said that the preclinical data indicate that it may reduce cell proliferation, increase tumour cell apoptosis and inhibit angiogenesis.

Lilly has now started a phase III trial of enzastaurin in patients with relapsed glioblastoma multiforme. It is being studied in other tumour types, including non-Hodgkin's lymphoma, colorectal cancer, non-small cell lung cancer, pancreatic cancer and mantle cell lymphoma.

NICE issues guidance on skin cancer services...

The UK's National Institute for Health and Clinical Excellence (NICE) and the National Collaborating Centre for Cancer (NCCC) have issued guidance on the planning, commissioning and configuration of healthcare services for people with skin tumours (www.nice.0rg.uk/csgstim).

The guidance brings community services – GPs – into the system which, NICE says "will ensure that the care provided to patients is tailored appropriately to the level of risk that their condition poses and that NHS resources are used in the most effective way".

NICE recommends that cancer networks should establish two levels of multidisciplinary teams: local hospital skin cancer teams and specialist skin cancer teams. People with precancerous skin lesions may be treated entirely by their GP. Those with low-risk basal cell carcinoma (BCCs) may be treated and followed up by a GP with a special interest, working within one of the multidisciplinary teams. All patients with suspicious pigmented skin lesions or a lesion that may be a high-risk BCC, squamous cell carcinoma or malignant melanoma should be referred to a specialist.

... and appraises bowel cancer treatment

NICE has also published a final appraisal determination (FAD) for the adjuvant treatment of patients with stage III (Duke's C) colon cancer, following surgery. The FAD recommends two options: either oxaliplatin (Eloxatin), in combination with 5-fluorouracil (5-FU) and folinic acid (FA); or capecitabine as monotherapy. Final guidance was due in April 2006.

EUROFILE

Lukewarm Response to Proposed Institute of Technology

European Commission plans to boost research through a European Institute of Technology (EIT) received a lukewarm reception when they were announced in February 2006. Intended to be a direct rival of the US MIT (Massachusetts Institute of Technology), the Institute forms another plank in the Commission's strategy (the 'Lisbon agenda') to improve competitiveness in Europe.

"Excellence needs flagships – that's why Europe must have a strong European Institute of Technology, bringing together the best brains and companies, and disseminating the results throughout Europe", said Commission President José Manuel Barroso at the launch. The Campaign for Parliament Reform – a group that lobbies for reform to the European Parliament's working methods – has suggested that the EIT should be situated in the parliament buildings in Brussels. But it seems more likely to emerge as a network of universities and other organisations, without a single site; partnerships in which members of research groups spend time in each other's labs. The launch is planned for the academic year 2009–10, assuming agreement at the next European Council meeting.

Barroso has said that it will be important to avoid reinventing the wheel and to pool existing European resources. But scientists are worried and sceptical, and some member states have already expressed their reluctance to get involved. At a meeting with Research Commissioner Janez Potocnik in February 2006, German science ministers said that they would prefer extra funding for existing leading German universities to the idea of the EIT. According to DG Education and Training, last year's consultation on this subject showed approval of the EIT coming mainly from central and eastern Europe and, to a lesser extent, southern Europe, with the north and west of Europe much less enthusiastic. It seems likely that this is a reflection of the existing state of international network development within each country.

''EXCELLENCE NEEDS FLAGSHIPS: EUROPE MUST HAVE A STRONG EIT''

Ministers on the Competitiveness Council, which includes research, failed to support the proposed EIT at a meeting in Brussels on March 13, 2006. Germany and the UK, in particular, were unconvinced by Commission President Barroso's plans. As a result, the Council summit later the same month was expected to defer a decision. "Diverse and decentralised organisations are one of the strengths of European science", said the German research ministry in a statement. "Quite fundamental questions on legal, financial and technical aspects as well as the question of European added value remain to be addressed. The government does not wish to decide on this issue at this stage through the European Council".

Although some companies are reported to have expressed an interest, many scientists fear that the EIT will divert money away from existing research funding schemes. MIT has an annual budget of $2bn, and it seems unlikely that anything remotely approaching that figure will be available. The Commission has not yet set a budget or given any indication of the kind of money it would like to see available, but says that funding will come from both public and private sectors. The public sector contribution most concerns European scientists. Chancellor of Oxford University, UK, and former European Commissioner Chris Patten argues that the Commission should concentrate its funds on existing institutions. He believes that the EIT would undermine the proposed European Research Council (ERC), created for much the same purpose.

However, Helga Nowotny, formerly chair of the European Research Advisory Board (EURAB), which advises the Commission, and vice-chair of the ERC, was reassured that the EIT would not divert funds from the ERC: "The EIT is not in Framework 7 and so will not affect the budget of the ERC". But she wondered how the EIT would persuade universities and industry to second staff and infrastructure to the EIT. This could work at national level, but would be hugely complicated at EU level, she said. Unlike MIT, which is concentrated on one site, 25 countries would be involved and it would be difficult to find a system that would work for all of them. In addition, she says that networks of technical universities already exist. "Europe doesn't need another network".

The Commission retorts that EIT networks will be different. "A fundamental difference between an ordinary 'network' and knowledge communities is that while in ordinary networks, these partners merely agree to co-operate, in the EIT communities, they will second resources to the EIT", say their plans. "Knowledge communities will cease to be part of their own organisation, and will become legally part of the EIT. Staff in a knowledge community will have a common management and performance-based evaluation process under the direction of the EIT. Knowledge communities will be flexible in order to allow new members to enter at different stages of activity, and to allow communities to change strategic direction. "During its lifetime a knowledge community could develop in a number of ways: flexibility must be built into the system".

''AN ILL-PREPARED POLITICAL RUSH JOB''

Many details of how the EIT will operate have yet to be decided. But there are already plans for its governance – through a centrally located body that would be responsible for priority-setting, managing the budget, and oversight of technology transfer and IPR. The Commission's proposals say that the board, drawn from academia and industry, should be autonomous, but that it will need to consider how the EIT will "balance accountability and the independence needed to enable it to manage its core business".

It remains to be seen whether the European Council meeting will take the view that the EIT is a real step to improving European competitiveness, or whether they will consider the proposals to be the "ill-prepared political rush job" that Nowotny sees.

Mary Rice
Brussels

Further plans announced for national biobanks

2006 might become the year of the biobank, thanks to two new initiatives announced by the US National Institutes of Health (NIH), and to the continued development of the UK biobank and similar projects in countries such as Japan and Sweden.

On February 8th, 2006, NIH launched the Genetic Association Information Network (GAIN) and the Genes and Environment Initiative (GEI). GAIN is a private-public partnership that has been launched with US$20 million for genotyping of five common diseases initially. GEI is scheduled to receive $68 million from federal funds to enable NIH-based research to combine analysis of genetic variation in patients with development of technology for monitoring of environmental exposures (e.g. wearable sensors). Both initiatives will use whole-genome association studies to genotype small-nucleotide polymorphisms, and will complement The Cancer Genome Atlas, which was announced in 2005.

A peer-review committee will decide on target diseases to be studied by researchers worldwide who, from later this year, can apply online to receive support from the initiatives. Data from GAIN and GEI will be put into databases managed by the National Centre for Biotechnology information. "You can expect, on the basis of the initiatives we announce, an avalanche of discoveries over the next 2–3 years", says Francis Collins (National Human Genome Research Institute, Bethesda, MD, USA). At the launch, NIH Director Elias Zerhouni said NIH has cohorts of patients that are well characterised and will focus the initiatives on more than 100 ongoing case-control population studies.

The UK biobank, which has been in planning since 2000, and is estimated to cost UK £60million, aims to recruit 500,000 volunteers aged 40–69 years to assess the interplay between environmental exposure, genetics, and the risk of chronic diseases such as cancer. "Studies to date have typically been characterised by small numbers of disease cases, incomplete or inadequate measures of potential risk factors and confounding factors, and retrospective case-control designs", explains UK biobank principle investigator, Rory Collins. "To help determine, and assess quantitatively, the main avoidable causes of various chronic diseases, there is now a strategic need to establish some large blood-based prospective epidemiological studies with prolonged follow-up of mortality and major morbidity".

In February 2006, UK biobank organisers began a pilot phase to assess the planned procedure and to ensure a widely representative population of volunteers before full-scale recruitment starts. Volunteers will give signed informed consent; complete a touch-screen computer-based questionnaire and short face-to-face interview; have biometric measurements; and give samples of blood and urine. Biobank organisers hope that tens of thousands of volunteers will have repeat assessments every few years.

Routine medical records or other relevant records will be used to follow-up volunteers for many decades. Data for deaths and cancer incidence will be obtained by linkage to the National Health Service [NHS] central registry and UK Office for National Statistics. Medical researchers will be able to use these data on approval by the biobank organisers and by the Ethics and Governance Framework (EGF), which was established with the project. Collins anticipates that much of the research will be based on nested case-control studies.

Sir John Sulston (Sanger Institute, Cambridge, UK) is excited by the open-ended nature of the project. "It will provide unanticipated leads, and answer questions that we haven't thought of yet", he says. But Mae-Wan Ho (Institute of Science in Society, London, UK) is concerned about the focus of so many resources on genomics alone. "Genomic fluidity and the layers of epigenetic complexity will frustrate any attempt to pin gene sequences to disease propensities, especially those, like cancer, that have a large environmental component".

Participants to UK biobank will give broad informed consent for use of their samples in future, as-yet unspecified research. Data will be stored in a central facility, to which a limited number of UK biobank staff will have access. Information that could identify people will be removed from data and samples at the earliest opportunity, and only staff with access to a secure code will be able to link them again.

In Japan, a personalised-medicine project started in June 2003, with the support of the government. The project aims to identify disease-susceptibility genes, molecular targets for drugs, and gene-environment interactions by obtaining serum, DNA, and clinical data for 300,000 patients with 47 common diseases by the end of 2007. By January 15, 2006, more than 130,000 patients had given written informed consent for participation in the project once a year. Yusuke Nakamura from the Human Genome Centre, University of Tokyo, Japan, hopes that the biobank will lead to the screening and validation of biomarkers to detect disease at an early or presymptomatic stage.

Researchers in Sweden are planning a project called Life Gene, which aims to follow-up 500,000 Swedish people by use of the internet and a biobank. Jan-Eric Litton (Karolinska Institute, Sweden) says registries in Sweden are an important resource: for example, the cancer registry and twin registry.

Litton has regular meetings with UK biobank "and I think we can learn from each other". UK biobank will receive scientific advice on an annual basis from an international advisory board. Although biobank strategies around the world differ, their common goal can be summarised by Zerhouni's conclusion to the new US initiatives: the greatest hope of controlling rapidly rising health-care costs is to usher in an era of medicine that is predictive, personalised, and pre-emptive.

Claire Tilstone

The full version of this story appeared in Lancet Oncol 2006 **7**:195–6.

PODIUM

The future of radiotherapy

Professor Michael Baumann

Michael Baumann is a Professor of Radiation Oncology at University of Dresden, Germany. His research interests include treatment of lung cancer, clinical radiobiology and tumour radiobiology. He is a former member of the FECS' Education Committee and became President of European Society for Therapeutic Radiology and Oncology (ESTRO) in 2005.

What's new in radiotherapy?

First, it's a boom time for developments in technology. New imaging techniques are improving the identification and location of tumours; also, PET scans allow information on the biology of the tumour to be integrated into treatment planning. With image-guided radiotherapy, data is collected and in-room imaging allows radiotherapy to be adjusted as it is carried out. High precision radiotherapy which hits the tumour and spares normal tissues has become a clinical reality with 3D conformal radiotherapy and, more recently, intensity modulated radiotherapy (IMRT). There are proton treatments and ion treatments that need to be evaluated for their clinical benefit. Overall, the technological developments are huge.

Second, new discoveries in cellular biology and molecular biology are having a profound effect. In this context, we are not looking simply for efficient drugs but for interactions of drugs and radiotherapy. Some drugs will make tumours more radiosensitive; others could make normal tissue more radioresistant and reduce the damage caused by radiotherapy. Site-specific research programmes will be needed to find drugs which specifically target the radiobiological mechanisms underlying the radioresistance of tumours. In addition, biological markers need to be identified for individually tailoring such combined treatment approaches.

Third, there is a strong and necessary move towards interdisciplinary oncology including radiotherapy, surgery and medical oncology. All disciplines have to see how they can best integrate with all the others. Most cancer patients receive a combination of therapies; we need to think about the best way to integrate them all.

Does radiotherapy receive proper recognition?

In many hospitals with a strong radiotherapy department, radiotherapy has a high standing. But awareness of radiotherapy's potential could be better, even among doctors. Organ and function sparing approaches will increase radiotherapy's importance, as will the changing demographics, because radiotherapy has advantages for older patients. We need to attract the most talented young people into this thrilling specialty. You need the same sound education in biology, diagnosis and treatment of cancer as in medical oncology but on top of that, skills in modern technology and physics.

How widespread is site-specific radiotherapy?

In northern and some central European countries, radiotherapy centres tend to be big and departments have a high degree of specialisation. That would also be true in big centres in other European countries such as Germany. However, Germany for example also has many smaller centres with less specialisation, and the disadvantages of it are clear: tough clinical decision-making and treatment application in difficult cases require a specialist consultant. On the other hand, for more straightforward, easier radiotherapy, for patients who don't live near the big centres, small centres provide a service. The overall quality of treatment must be ensured, and everyone needs to know and accept the limits of the treatment they can offer.

How well do the various disciplines work together?

In integrated centres, specialties educate each other at professional level on a daily basis. But we need to do more. Medical students would benefit from a joint course in cancer treatment, taught by different specialists. In Dresden, we run a successful interdisciplinary problem-oriented course over 8 weeks, entirely dedicated to oncology.

Someone training in radiation oncology would benefit from experience in medical oncology or surgery and vice versa. The aim is not to produce generalists – the field is too complicated not to specialise and we do not need radiation oncologists to become expert surgeons. But we need to foster understanding of the advantages each field has to offer.

How wide is the variation in radiotherapy provision across Europe?

ESTRO ran a survey across the European Union, QUARTS, which looked at equipment and staffing levels in relation to an estimate of the cancer incidence for the local population. The availability of radiotherapy varies widely, and in general terms, countries new to the EU and applicant states in central Europe have the least provision. However, there is also a lack of infrastructure and staffing in some Western European countries. We are working to improve that and to ensure access to high quality radiotherapy all over Europe.

Presumably the economics is a factor here?

Start up costs are a problem. A single linear accelerator, plus the room to house it, could easily cost 5 million Euro, a big chunk of money. But if you look over the longer term, at the number of patients treated over the 10–15 years of a linear accelerator's lifespan, it is a very cost effective treatment.

What do you hope to achieve in your 2 years as ESTRO President?

For ESTRO to promote integrated care across the whole of Europe. We have to create equal access to high quality radiotherapy for all. This requires efforts in research as well as in education and training. New scientific developments need to be investigated and judged and ESTRO needs to make recommendations to health care providers and governments about the benefits of this technology, urging increased access. At the same time, we need to make clear to other oncology specialists what benefits they can expect from radiotherapy now, and in the future. To accomplish this, we need interdisciplinary structures throughout Europe.